

Full Report from ASCO 2018

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This issue of Onco-this-Week presents 50+ updates from ASCO 2018 meeting (Chicago, IL) which includes several studies like DUO, MAVORIC, ADMYRE, KEYNOTE-006, -042, -158, 184, -427, -524, -526, TOPACIO, QUADRA, ARCHER 1050, VISION, EMPOWER-CSCC-1, ZUMA-1, -3, COLUMBUS, Study 08, CAPTIVATE, RELEVANCE, MONALEESA-3, ALEX, CELESTIAL, Checkmate-227, JAVELIN Merkel 200, TRANSCEND, MURANO, OPTIMISM, ICONIC, IMPACT, SANDPIPER, LIBRETTO-001, ENESTop and ENEST freedom trials.

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1. [Verastem Oncology presents data on two lead drug candidates](#)

- Duvelisib demonstrates robust clinical activity with 73% ORR and a median of 15 month PFS in the DUO crossover study of patients who became relapsed/refractory to ofatumumab in DUO™
- Duvelisib’s dual inhibition of PI3K-delta and PI3K-gamma results in beneficial changes in both the cancer cells and the supportive tumor microenvironment
- Phase I results show defactinib in combination with pembrolizumab and gemcitabine is well tolerated and shows early signs of clinical activity in pancreatic cancer including confirmed partial response and long-term stable disease

Jonathan Pachter, PhD, Chief Scientific Officer of Verastem Oncology, commented, “The presented research by Drs. Casulo and Weaver continues to provide important evidence that the dual PI3K-delta/PI3K-gamma inhibitory activity of duvelisib results in beneficial anti-tumor effects on both the

cancer cells and their supportive tumor microenvironment (TME) which has the potential to enhance clinical efficacy and improve outcomes for patients battling CLL/SLL and FL.”

2. Kyowa Kirin presents new data for Mogamulizumab from Its lead program in Cutaneous T-cell Lymphoma (CTCL)

Progression free survival (PFS) was the primary endpoint; the results that demonstrated mogamulizumab had a clinically relevant and statistically significant increase in progression free survival over vorinostat have already been presented. Infusion reaction and rash were the most common adverse events associated with mogamulizumab. QOL measurements were secondary endpoints and included Skindex29 (SDX-29), Functional Assessment of Cancer Therapy-General (FACT-G) and EuroQol-5D. SDX-29 and FACT-G were reported in ASCO.

“Quality of life may be severely impacted in patients living with CTCL, and the MAVORIC study included evaluation of the effect of both treatments on a range of QOL instruments,” said Jeffrey S. Humphrey, M.D., President of Kyowa Kirin Development. “We are encouraged by the QOL data and look forward to working with investigators and patient advocates to further understand how mogamulizumab might help patients with MF and SS.”

3. PharmaMar presents in oral session at ASCO the ADMYRE study’s adjusted overall survival with plitidepsin

- The modelled data on overall survival of the statistical evaluation of the impact of crossover on the ADMYRE study were presented.
- Of the 84 patients treated in the comparator arm (dexamethasone as a single agent), 44% received the combination with plitidepsin after progression.
- After analyzing the impact of crossover, the registered overall survival with plitidepsin was 11.6 months against the 6.4 months of dexamethasone alone.

The primary endpoint of this study was Progression Free Survival -which resulted to be positive- was to demonstrate a statistically significant reduction in the risk of disease progression or death of 35% against the comparator.

During the presentation, the 2 statistical models used (RPSFT and the two stage method) to correct and measure the impact of crossover on overall survival were discussed, emphasizing the two stage model (Latimer et al.), that was considered the most adequate in the context of the Admyre study..

Accordingly, and taking into account the effect of crossover using the two stage method, a statistically significant increase in overall survival in the plitidepsin plus dexamethasone arm (11.6 months) against the comparator (6.4 months) was observed.

4. Dynavax reports data for Ph 1b/2 trial of SD-101 in combination with pembrolizumab in Advanced Melanoma

- Overall response rate (ORR) of 70% (21 of 30), with a complete response (CR) rate of 17%, for advanced melanoma patients who received the ≤ 2 mg dose of SD-101 in up to four lesions
- ORR of 38% (15 of 39) in patients who received the 8 mg dose of SD-101 in one lesion
- Durable response in patients who received ≤ 2 mg dose of SD-101 with 74% 6-month progression free survival (PFS) rate
- Observed responses in injected lesion(s) and distant lesions, including visceral metastases in the liver
- Responders included 8 of 10 PD-L1 negative patients in the ≤ 2 mg dose cohort
- AEs related to SD-101 treatment were transient, mild to moderate flu-like symptoms at both the ≤ 2 mg and the 8 mg dosing levels
- No increase in the frequency of immune-related adverse events over individual monotherapies reported in other studies^{1,2} nor evidence of any new safety signals

5. [PharmaMar presents new results with lurbinectedin as a single agent in patients with recurrent small-cell lung cancer](#)

- The phase II basket trial, which began recruiting 15 patients with recurrent small-cell lung cancer, was increased to target enrolment of 100 after obtaining a positive response.
- In a total of 61 patients, an objective response has been observed in 39.3% of them, with a median duration of response of 6.2 months and a median overall survival (OS) of 12 months.
- The primary endpoint of the study is objective response rate (ORR), with other secondary endpoints, including duration of response, progression free survival, overall survival and safety profile.

“The patients included in this study with small-cell lung cancer are responding favorably to the treatment with lurbinectedin as a single agent. We have observed that this molecule is active in this group of patients, however, we look forward to having more information once recruitment has finalized and we can evaluate all the patients”, said Dr. Arturo Soto, Director of Clinical Development at the Oncology Business Unit of PharmaMar.

6. [TESARO summarizes TOPACIO and QUADRA trial results](#)

- TOPACIO data for ZEJULA® (niraparib) in combination with an anti-PD-1 mAb highlight promising activity in platinum-resistant/refractory ovarian cancer and triple-negative breast cancer beyond patients with BRCA mutations and support initiation of registration trials
- QUADRA results demonstrate durable responses beyond patients with BRCA mutations in late-line ovarian cancer treatment setting and support label expansion

“The promising data presented at this year’s ASCO meeting demonstrated the potential of ZEJULA not only as a monotherapy treatment for women with advanced ovarian cancer, but also in combination with an anti-PD-1 antibody, to provide a meaningful clinical benefit to patients beyond those with *BRCA* mutations,” said Mary Lynne Hedley, Ph.D., President and COO of TESARO. “Our oncology development strategy is focused on rational therapeutic combinations and niraparib and TSR-042, our anti-PD-1 antibody, are the foundation of this strategy. The TOPACIO results support the advancement of combination studies in ovarian cancer and breast cancers and we have initiated preparations for registrational trials of niraparib in combination with TSR-042 in these settings.

QUADRA results demonstrated that ZEJULA is active as a late-line treatment for patients beyond those with *BRCA* mutations, which is the only treatment setting in which PARP inhibitors are approved today, and we intend to submit an sNDA in the fourth quarter of 2018."

[7. Dacomitinib Shows More than Seven-Month Improvement in Overall Survival Compared to an Established Therapy in Advanced NSCLC with EGFR-Activating Mutations](#)

The trial showed a median OS of 34.1 months for patients receiving dacomitinib (95% CI: 29.5, 37.7), representing a more than seven-month improvement compared to 26.8 months with gefitinib (95% CI: 23.7, 32.1). The OS data from ARCHER 1050 were presented today as an oral presentation [Abstract #9004] at the 54th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago and have been published simultaneously in the *Journal of Clinical Oncology*.

"Overall survival is an important measure to assess efficacy of investigational compounds. These data presented today are particularly significant as dacomitinib is the first EGFR tyrosine kinase inhibitor in a Phase 3 head-to-head study comparing two tyrosine kinase inhibitors to show an improvement in overall survival," said Professor Tony Mok, Chair of Department of Clinical Oncology, The Chinese University of Hong Kong. "I look forward to having dacomitinib as a potential first-line treatment option for non-small cell lung cancer patients with EGFR-activating mutations."

[8. NewLink Genetics Announces Final Results from Two Phase 2 Studies of Indoximod Presented at ASCO 2018](#)

Indoximod in combination with checkpoint inhibition in advanced melanoma

Results from a single-arm Phase 2 study of indoximod in combination with checkpoint inhibitors for patients with advanced melanoma were presented today by Yousef Zakharia, MD, Assistant Professor of Medicine, Division of Hematology, Oncology and Blood & Marrow Transplantation at the University of Iowa and Holden Comprehensive Cancer Center.

In this [study](#), of 102 total patients enrolled, 101 patients with advanced melanoma were treated with indoximod plus standard-of-care checkpoint inhibition as approved for melanoma. 70 patients with cutaneous or mucosal melanoma were treated with pembrolizumab plus indoximod and had an on-treatment imaging, meeting the per-protocol, pre-specified definition of evaluable for efficacy. Of the remaining 32 patients, 15 had uveal melanoma, 4 received ipilimumab, 4 received nivolumab, and one patient was never treated. In addition, 8 patients came off study prior to the first on-treatment imaging study. The full data set, including the expanded biopsy cohort, is provided on the company's website in the "[Posters & Presentations](#)" section under the "Investors & Media" tab. Key findings from the 70 evaluable for efficacy patients presented from the study include:

- ORR for combination therapy of 56%
- CR of 19%
- Median PFS of 12.4 months
- PD-L1 \geq 1% staining of 54% (22/41 patients with archival tissue)
- ORR by PD-L1 status
- PD-L1 (+) patients: ORR of 77%
- PD-L1 (-) patients: ORR of 42%
- Combination was well tolerated

Indoximod in combination with chemotherapy in metastatic pancreatic cancer

Results from a Phase 2 study of indoximod plus chemotherapy for patients with metastatic pancreatic cancer were presented at ASCO by Nathan Bahary, MD, PhD, Associate Professor in the Division of Oncology and Medical Director of the Pancreatic Cancer Program at the University of Pittsburgh Medical Center. Key findings from this [study](#) show that the combination was well tolerated with a median Overall Survival (mOS) of 10.9 months and an Overall Response Rate (ORR) of 46.1%. Although the study did not meet the prespecified primary goal of a 30% decrease in the risk of death compared with historical controls, the combination demonstrated potentially promising activity with an immunologic correlation for response to therapy.

[9. Endocyte Announces Enrollment of First Patient in Phase 3 VISION Trial of 177Lu-PSMA-617 in Prostate Cancer](#)

“We are pleased to announce the initiation of this important clinical trial so quickly following our end-of-phase 2 meeting with the FDA. This speed of execution is a result of the enthusiasm of participating physicians and the focus and urgency of our clinical operations team,” said Mike Sherman, president and CEO of Endocyte. “Having collaborated with several of the key opinion leaders in prostate cancer around the world, we are confident in the robustness of the VISION trial design and eager to complete enrollment.”

[10. Adaptimmune presents detailed safety update from ongoing MAGE-A10 pilot studies](#)

Adaptimmune Therapeutics plc (Nasdaq:ADAP), a leader in T-cell therapy to treat cancer, presented a safety update from its two ongoing pilot studies with SPEAR T-cells targeting MAGE-A10 in non-small cell lung cancer (NSCLC) and the triple tumor study in bladder, melanoma, and head & neck cancers at the American Society of Clinical Oncology (ASCO) annual meeting.

“Based on these safety data, we are enrolling patients and dosing at the target dose of one billion transduced cells in both MAGE-A10 studies, and we anticipate response data later this year,” said Rafael Amado, Adaptimmune’s Chief Medical Officer. “Given our preclinical validation and safety testing data, as well as available clinical results, we anticipate that MAGE-A10 SPEAR T-cells will continue to have an acceptable safety profile as we dose patients in higher cell dose cohorts.”

Safety Update

A safety update from the two ongoing MAGE-A10 pilot studies was presented during a poster session (data cut-off 04 May 2018):

- Eight patients in the 100 million cell safety cohorts received MAGE-A10 SPEAR T-cells in the two ongoing pilot studies: 3 in Cohort 1 of the triple tumor study, and 5 in Cohort 1a of the NSCLC study
- Out of the eight patients treated in the safety cohorts, seven received 100 million transduced SPEAR T-cells, and one patient in the triple tumor study received 90 million cells
- There were no deaths attributable to SPEAR T-cell therapy
- To date, there has been no evidence of off-target toxicity
- There were two events of cytokine release syndrome (CRS), both in the NSCLC study: one Grade 4 and one Grade 1; both events resolved

- The Grade 4 event of CRS was considered a dose limiting toxicity (DLT), at the time, and cohort 1a of the NSCLC study was expanded from 3 to 6 patients
- Overall, most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies
- While no anti-tumor effects were observed at the 100 million cell dose level, transduced SPEAR T-cells were detectable in peripheral blood
- Although cells were readily detectable, observed SPEAR T-cell peak expansion was approximately tenfold lower than what was seen at doses of at least one billion cells in other studies, such as those with NY-ESO SPEAR T-cells

After review of these initial safety data by the safety review committee (SRC), the decision was made to escalate to the next dose of one billion transduced MAG-EA10 SPEAR T-cells in the triple tumor and the NSCLC study. One billion cells was the therapeutic threshold dose observed with SPEAR T-cells targeting NY-ESO in the synovial sarcoma pilot study.

Response data from these ongoing studies is anticipated throughout the remainder of 2018.

NSCLC Study:

- o Patients must be at least 18 years of age and have Stage IIIb or IV NSCLC, have failed at least one platinum-containing regimen (may have received CPDs), have measurable disease, ECOG 0-1, adequate organ function, and be without brain metastases, history of severe autoimmune disease or current uncontrolled illness
- o The lymphodepletion regimen for patients receiving:
 - 100 million transduced cells was cyclophosphamide alone (1800 mg/m²/day) for 2 days
 - One billion (1.0 x 10⁹) transduced cells is cyclophosphamide 600mg/m²/day and fludarabine 30 mg/m²/day on Days -7, -6 and -5
 - One to six billion (1-6 x 10⁹) or up to ten billion (1.0 x 10¹⁰) transduced cells is cyclophosphamide 600mg/m²/day on Days -7, -6, -5 and fludarabine 30 mg/m²/day on Days -7, -6, -5, and -4
- o Efficacy is assessed by response rate, duration of response, progression-free survival, and overall survival at weeks 4, 8, and 12, month 6, and then every 3 months (for 2 years) and then every 6 months until confirmation of disease progression

Triple Tumor Study:

Patients must be at least 18 years of age and have inoperable or metastatic (advanced) urothelial “bladder” cancer, melanoma, or squamous cell head and neck tumors; and, have received standard of care therapies and have progressive disease

The lymphodepletion regimen for patients receiving:

- 100 million transduced cells was cyclophosphamide 600mg/m²/day and fludarabine 30 mg/m²/day on Days -7, -6 and -5
- One billion (1.0 x 10⁹) transduced cells is cyclophosphamide 600mg/m²/day and fludarabine 30 mg/m²/day on Days -7, -6 and -5

- One to six billion (1-6 x 10⁹) or up to ten billion (1.0 x 10¹⁰) transduced cells is cyclophosphamide 600mg/m²/day on Days -7, -6, -5 and fludarabine 30 mg/m²/day on Days -7, -6, -5, and -4

Efficacy is assessed by overall response rate, best overall response, time to response, duration of response, duration of stable disease, progression-free survival, and overall survival at weeks 6, 12, 18, and 24 weeks, and then every 3 months until confirmation of disease progression

11. Kite Announces Initial Results From a Phase 1 Study of T Cell Receptor (TCR) Cell Therapy in HPV-16-Positive Solid Tumors

In this study, eight patients with metastatic HPV-16 cancers received a single infusion of gene-engineered E7 T cells at one of three dose levels. Patients had received between three and seven prior lines of systemic cancer therapy. In the initial six patients, the E7 TCR was expressed by 90-99 percent of the infused T cells, and E7 T cells were detectable in the peripheral blood six weeks following treatment. The study is ongoing.

Partial responses (Response Evaluation Criteria in Solid Tumors (RECIST); RECIST 1.1) were observed in three out of the seven evaluable patients and another two patients had stable disease. To date, the responses have lasted as long as nine months and have occurred in patients with vulvar, oropharyngeal and anal cancer. Two of these patients had been previously treated with anti-PD1 checkpoint blockade.

“Metastatic HPV-cancers are incurable and poorly addressed by standard therapies,” said Christian S. Hinrichs, MD, Lasker Clinical Research Scholar at the Center for Cancer Research’s Experimental Transplantation and Immunology Branch (ETIB) at the NCI and lead study investigator. “The early results from this Phase 1 trial support the continued evaluation of TCR therapy in HPV-associated cancers.”

12. First presentation of LENVIMA/KEYTRUDA data in patients with unresectable HCC, which aims to be the first systemic combination of a TKI and immunotherapy for these patients, as well as SCCHN

- Updated results show antitumor activity with a consistent safety profile in advanced renal cell carcinoma (RCC) and advanced endometrial carcinoma (EC)
- The LENVIMA/KEYTRUDA combination was recently granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy Designation for advanced RCC
- Phase 3 trials underway in advanced RCC (NCT02811861) and advanced EC (NCT03517449)

Early phase results from Study 116/KEYNOTE-524 support further investigation in unresectable HCC

Study 116/KEYNOTE-524 is a Phase 1b open-label, single-arm multicenter study evaluating the tolerability and safety of the combination of LENVIMA (12 mg/day for patients weighing ≥ 60 kg, 8 mg/day for patients weighing < 60 kg) and KEYTRUDA (200 mg intravenously every 3 weeks) in patients with unresectable HCC, Barcelona Clinic Liver Cancer (BCLC) stage B (not eligible for transarterial chemoembolization [TACE]) or C, Child-Pugh class A, and ECOG performance status of 0

or 1. The primary endpoint was safety; secondary and exploratory endpoints included overall survival (OS), objective response rate (ORR), progression-free survival (PFS) and time to progression (TTP) using modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria. Tumor assessments of complete or partial response (CR or PR) were confirmed greater than or equal to four weeks after initial response. Part 1 evaluated tolerability by assessing dose-limiting toxicities (DLTs) during the first cycle of treatment in patients for whom no other appropriate therapy was available. After tolerability was confirmed, additional patients with no prior systemic therapy for unresectable HCC were enrolled (Part 2). The expansion part of the study will evaluate objective response rate and duration of response as measured by mRECIST.

Data presented at ASCO are from one abstract:

- *A Phase 1b trial of lenvatinib (LEN) plus pembrolizumab (PEM) in patients (pts) with unresectable hepatocellular carcinoma (uHCC) (Abstract #4076)*

As of March 22, 2018, 30 patients were enrolled in this trial (Part 1, n=6; Part 2, n=24). No dose-limiting toxicities were reported. Four patients discontinued due to treatment emergent adverse events (TEAEs). The most common TEAEs (any grade) were decreased appetite (53.3%) and hypertension (53.3%), diarrhea (43.3%) and fatigue (40.0%). Tumor assessments were performed according to mRECIST by the investigators. At data cutoff, the ORR (including cases of unconfirmed CR and PR) was 42.3% (95% CI: 23.4-63.1). A second scan was performed at least four weeks following the initial response, which demonstrated a confirmed ORR of 26.9% (95% CI: 11.6-47.8). Median duration of PFS was 9.7 months (95% CI: 5.55-NE). None of the treated patients experienced progressive disease (PD) as best overall response (BOR). Twenty-three patients (Part 1, n=3, Part 2, n=20) are still undergoing study treatment. Based on the safety and efficacy data seen thus far, the protocol has been amended to enroll approximately 94 patients to the Part 2 expansion cohort.

New and updated results from Study 111/KEYNOTE-526 support further evaluation in SCCHN, RCC and EC, as well as biomarker analysis with clinical serum samples from patients with advanced EC to clarify combination rationale

Study 111/KEYNOTE-526 is a multicenter, open-label, single-arm Phase 1b/2 basket trial evaluating the combination of LENVIMA (20 mg/day) with KEYTRUDA (200 mg intravenously every three weeks) in patients with selected solid tumors. Patients were not preselected based on PD-L1 status. The primary endpoint of the Phase 1b study was to determine the maximum tolerated dose of KEYTRUDA and LENVIMA in combination. The primary endpoint of the Phase 2 portion is investigator-assessed ORR at week 24 based on immune-related RECIST (irRECIST). The secondary efficacy endpoints included ORR, PFS, and duration of response for patients with complete or partial responses.

Data presented at ASCO are from four abstracts:

- *A Phase 1b/2 trial of lenvatinib plus pembrolizumab in patients with squamous cell carcinoma of the head and neck (Abstract #6016)*

As of December 1, 2017, 22 patients with measurable, confirmed metastatic SCCHN and ECOG performance status of 0 or 1 were enrolled in this cohort. 90.9% of patients received at least one prior anticancer therapy. At data cutoff, ORR at week 24 was 36.4% (95% CI: 17.2-59.3), overall ORR was 40.9% (including 1 CR and 8 PRs; 95% CI: 20.7-63.6), and PFS rate at 12 months was 41.9% (95% CI: 17.6-64.7). None of the treated patients experienced progressive disease (PD) as best overall response (BOR), and tumor size reduction was observed in the majority of the patients. Grade 3 or 4

TRAEs occurred in 72.7% of patients (Grade 4 TRAEs in 4.5%). The most common TRAEs (any grade) were fatigue (50.0%), hypertension (40.9%), diarrhea (36.4%), decreased appetite (31.8%), oropharyngeal pain (31.8%) and stomatitis (31.8%). Overall, the study demonstrated promising clinical activity, supporting further evaluation of the combination in patients with SCCHN.

- *Lenvatinib + pembrolizumab in patients with renal cell carcinoma: updated results (Abstract #4560)*

This cohort enrolled 30 patients with metastatic clear cell RCC and measurable disease per irRECIST. In addition to the assessments performed by investigators per irRECIST, these updated data include tumor assessments performed retrospectively by independent radiographic review (IRR) per irRECIST and RECIST 1.1, as well as the first report of PFS results in this cohort. ORR at week 24 was 63.3% (95% CI: 43.9–80.1), based on investigator assessment per irRECIST. At data cutoff on December 1, 2017, overall ORR was 70.0% (95% CI: 50.6-85.3) based on investigator assessment per irRECIST; median duration of response was 18.4 months (95% CI: 10.3-NE), and median PFS was not estimable (95% CI: 11.6-NE). Based on the IRR per irRECIST, ORR was 66.7% (95% CI: 47.2-82.7), median duration of response was not estimable (95% CI: 14.9-NE), and median PFS was 18.0 months (95% CI: 10.2-NE); per RECIST 1.1, ORR was also 66.7% (95% CI: 47.2-82.7), median duration of response was 16.6 months (95% CI: 8.9-NE), and median PFS was 18.0 months (95% CI: 9.6-NE). Grade 3 or 4 AEs occurred in 22 patients (73.3%), and eight patients (26.7%) discontinued treatment due to an AE. The most common AEs (any grade) were diarrhea (83.3%), fatigue (73.3%), hypothyroidism (70.0%), stomatitis (63.3%) and nausea (60.0%). A Phase 3 trial comparing the LENVIMA plus KEYTRUDA combination and the LENVIMA plus everolimus combination versus sunitinib monotherapy for the first-line treatment of advanced RCC is currently recruiting (CLEAR; NCT02811861; please visit clinicaltrials.gov for more information).

- *Lenvatinib + pembrolizumab in patients with advanced endometrial cancer: Updated results (Abstract #5596)*

As of data cut-off of December 15, 2017, efficacy and safety analyses are summarized in the poster for 53 patients with histologically confirmed metastatic EC, irrespective of microsatellite instability (MSI) or mismatch repair (MMR) status, and measurable disease per irRECIST. Four (7.5%) patients were MSI-high, 45 (85%) were non MSI-H (MSS), and four (7.5%) patients' MSI status was not known. At data cutoff, ORR at week 24 based on investigator assessment was 39.6% (95% CI: 26.5-54.0); overall ORR was the same. Objective responses were seen regardless of tumor MSI status. Confirmed objective responses were seen in patients with MSS tumors (16/45 [ORR 35.6%]; 95% CI: 21.9-51.2) and MSI-H tumors (2/4 [ORR 50.0%]; 95% CI: 6.8-93.2). Secondary analysis of tumor efficacy by independent radiology review (IRR) showed an ORR at week 24 of 45.3% (95% CI: 31.6-59.6) and an overall ORR of 47.2% (95% CI: 33.3-61.4) with 22 partial responses and three complete responses. Of responding patients, 83.0% (95% CI: 55.9-94.2) had a response duration of six months or more and 64.5% (95% CI: 32.8-84.2) had a response duration of 12 months or more per investigator assessment, and median duration of response had not yet been reached (95% CI: 7.4-NE). When assessed by IRR, among responding patients, 79.3% (95% CI: 48.5-92.9) had a response duration of 12 months or more, and median duration of response was also not yet reached (95% CI: 5.8-NE). Median PFS was 7.4 months (95% CI: 5.0-not estimable [NE]) per investigator assessment. Most patients showed a decrease in the mean maximum percentage change from baseline in the sum of the diameters of target lesions, regardless of MSI or PD-L1 expression status. Grade 3 treatment-related adverse events (TRAEs) occurred in 37 patients (70%); there were no Grade 4 TRAEs. Five patients (9%) discontinued treatment due to TRAEs. The most common TRAEs (any grade) were hypertension (59%), fatigue (55%), diarrhea (51%), hypothyroidism (47%), decreased appetite (40%), nausea (38%) and stomatitis (34%). A randomized, international, 2-arm, Phase 3

study in recurrent endometrial carcinoma is underway (Study 309/KEYNOTE-775; NCT03517449; please visit clinicaltrials.gov for more information).

- *Biomarker results and preclinical rationale for combination of lenvatinib and pembrolizumab in advanced endometrial carcinoma (Abstract #5597)*

In an exploratory analysis, 41 candidate serum biomarkers were assessed in immunoassay panels of serum samples collected at baseline, on cycle one, day 15 (C1D15); and cycle two, day one (C2D1) from 37 patients with EC receiving the LENVIMA plus KEYTRUDA combination. In patients with advanced EC, treatment with the combination was associated with changes in several serum biomarkers, including interferon (IFN)- γ and IFN- γ -regulated chemokines, some of which may be associated with tumor response. In addition to the exploratory analysis from Study 111/KEYNOTE-526, preclinical studies on the immunomodulatory and antitumor activity of LENVIMA when combined with PD-1/PD-L1 blockade were presented to more clearly define the basis of combination LENVIMA plus KEYTRUDA. The *in vivo* preclinical models suggest that LENVIMA monotherapy may decrease the population of tumor-associated macrophage in the tumor microenvironment and the combination therapy may act via a mechanism that includes the interferon signaling pathways to enhance antitumor activity over each monotherapy. Overall, these findings provide rationale for the antitumor activity of LENVIMA plus KEYTRUDA in combination.

13. Pivotal cemiplimab trials showing positive results in advanced cutaneous squamous cell carcinoma presented

Data published in NEJM and/or presented at ASCO, and confirmed by independent central review, include:

- **Phase 2 EMPOWER-CSCC-1 trial:**
 - o Cemiplimab-treated patients had a 47.5 percent response rate (28 of 59 patients, including 4 complete responses and 24 partial responses [PRs]) with a median observed time to response of 2 months as of the data cut-off date. The durable disease control rate (DCR) was 61 percent (36 of 59 patients) and was defined as the proportion of patients without progressive disease for at least 105 days.
 - o The median duration of response (DOR), median progression free survival, and median overall survival have not been reached as of the data cut-off date (median follow-up for all patients: 8 months). Of the responding patients, 82 percent remained in response and continued on cemiplimab. The estimated progression-free probability at 12 months was 52.5 percent, and the estimated probability of survival at 12 months was 81 percent.
 - o The most common treatment-emergent adverse events were diarrhea (27 percent), fatigue (24 percent), nausea (17 percent), constipation and rash (each 15 percent). Grade 3 or higher adverse events regardless of attribution were reported in 25 patients (42 percent), of whom seven (12 percent) were considered related to treatment. Three patients (5 percent) had adverse events with the outcome of death; however, none were considered related to treatment.
 - o Data are from 59 metastatic CSCC patients who received cemiplimab (3 mg/kg every 2 weeks) for up to 96 weeks.

- **CSCC expansion cohorts of Phase 1 trial:**

- o Cemiplimab-treated patients had a response rate of 50 percent (13 of 26 patients, all of which were PRs) with a median observed time to response of 2 months as of the data cut-off date. The durable DCR was 65 percent (17 of 26 patients). The median DOR has not been reached as of the data cut-off date (median follow-up for all patients: 11 months). The most common treatment-emergent adverse events of any grade were fatigue (27 percent), constipation, decreased appetite, diarrhea, hypercalcemia, hypophosphatemia, nausea and urinary tract infection (each 15 percent). Grade 3 or higher adverse events regardless of attribution were reported in 12 patients (46 percent), of which five (19 percent) were considered related to treatment. Two patients (8 percent) had adverse events related to treatment that led to treatment discontinuation.

- o Data are from 26 advanced CSCC patients who participated in two Phase 1 expansion cohorts and received cemiplimab (3 mg/kg every 2 weeks) for up to 48 weeks. Patients either had metastatic CSCC or locally advanced CSCC who were not candidates for surgery.

14. Merck's KEYTRUDA® (pembrolizumab) Showed Promising Anti-Tumor Activity in Patients with Advanced Small Cell Lung Cancer (SCLC) in Phase 2 KEYNOTE-158 Study

KEYNOTE-158 (ClinicalTrials.gov, NCT02628067) is an ongoing global, open-label, non-randomized, multi-cohort, multi-center, Phase 2 study evaluating KEYTRUDA in patients with multiple types of advanced solid tumors – including SCLC – that have progressed on standard of care therapy. The SCLC cohort of the study enrolled 107 patients, regardless of biomarker status, who received KEYTRUDA as monotherapy (200 mg fixed dose every three weeks). The primary endpoint was ORR as evaluated by independent central review using RECIST v1.1. Secondary endpoints are progression-free survival (PFS), overall survival (OS), duration of response (DOR) and safety.

In the overall SCLC patient cohort (n=107), data at ASCO showed an ORR of 18.7 percent (95% CI, 11.8-27.4), with a complete response rate of three percent and a partial response rate of 16 percent. Median DOR was not reached (range, 2.1+ to 18.7+ months) and 73 percent of patients had a DOR of 12 months or longer. Median PFS was 2.0 months (95% CI, 1.9-2.1) with six- and 12-month PFS rates of 23.7 percent and 16.8 percent, respectively. Median OS was 8.7 months (95% CI, 5.6-12.0) with six- and 12-month OS rates of 57.5 percent and 40.2 percent, respectively.

In the pre-specified, exploratory analyses based on PD-L1 status, patients whose tumors expressed PD-L1 (n=42) showed an ORR of 35.7 percent (95% CI, 21.6–52.0), with a complete response rate of five percent and a partial response rate of 31 percent. Additionally, median PFS was 2.1 months (95% CI, 2.0-8.1) with six- and 12-month PFS rates of 38.9 percent and 28.5 percent, respectively. Median OS was 14.9 months (95% CI, 5.6-NR) with six- and 12-month OS rates of 66.0 percent and 53.1 percent, respectively.

In patients whose tumors did not express PD-L1 (n=50), ORR was six percent (95% CI, 1.3-16.5), with a complete response rate of two percent and a partial response rate of four percent. Median PFS was 1.9 months (95% CI, 1.6-2.0) with six- and 12-month PFS rates of 14.3 percent and 8.2 percent, respectively. Median OS was 5.9 months (95% CI, 3.3-10.1) with six- and 12-month OS rates of 48.3 percent and 30.7 percent, respectively. In other pre-specified subgroup analyses, the ORR was generally consistent across clinically relevant subgroups, including patients (n=61) who had received two or more prior lines of therapy where the ORR was 23 percent (95% CI, 13.2-35.5).

The safety profile was consistent with what has been seen in previously reported studies of KEYTRUDA monotherapy in lung cancer. Treatment-related adverse events (TRAEs) occurring in 10 percent or more of patients were fatigue (14%), pruritus (12%), hypothyroidism (12%), decreased appetite (10%) and nausea (10%). Thirteen patients had grade 3-4 TRAEs; two deaths occurred due to TRAEs (pneumonia and encephalopathy). Immune-mediated adverse events and infusion reactions were reported in some patients. Hypothyroidism was the most commonly reported immune-mediated adverse event, followed by hyperthyroidism and severe skin reactions.

15. Kite announces new data analyses for CAR T therapy in patients with Blood Cancers

- ZUMA-1 Data Suggest Patient Response to Yescarta® (axicabtagene ciloleucel) at Three Months May be Predictive of Longer-Term Response in Refractory B-cell Lymphoma --
- ZUMA-3 Analysis Suggests High Complete Response Rates with KTE-C19 in Adult Patients with Relapsed or Refractory Acute Lymphoblastic Leukemia (ALL) Regardless of Prior Blinatumomab Treatment --

Ongoing Responses, Response by Prior Lines of Therapy in ZUMA-1 (Abstracts #3003 and #3039)

Long-term ZUMA-1 follow-up data have shown an overall response rate (ORR) of 83 percent (n=84/101), including 58 percent (n=59/101) of patients with a complete response at a median follow-up of 15.1 months. In this long-term follow-up, Grade 3 or higher cytokine release syndrome (CRS) and neurologic events were seen in 12 percent and 29 percent of patients, respectively.

A new analysis of ZUMA-1 suggests that response status three months after infusion of Yescarta may be predictive of longer-term disease control. Of the 42 patients with complete response and nine with partial response at three months, the 12-month PFS rates were 79 percent and 78 percent, respectively. This abstract has also been selected for inclusion in the 2018 Best of ASCO® program.

“We are encouraged by the strong long-term complete response rates in ZUMA-1, which represents a patient population that previously had few if any remaining treatment options,” said Frederick L. Locke, MD, ZUMA-1 Co-Lead Investigator and Vice Chair of the Department of Blood and Marrow Transplant and Cellular Immunotherapy at Moffitt Cancer Center in Tampa, Florida. “Importantly, this new study analysis indicates that response status at three months is potentially predictive of prolonged PFS.”

An additional ZUMA-1 analysis evaluated outcomes based on prior therapy the patients had received. The results indicate long-term clinical benefit for patients with refractory large B cell lymphoma, irrespective of the number of prior lines of therapy.

Rates of Response with Prior Blinatumomab Treatment in ZUMA-3 (Abstract #7006)

Phase 1 data for KTE-C19, an investigational CD19 CAR T cell therapy, presented at the 2017 Annual Meeting of the American Society of Hematology (ASH) demonstrated high rates of complete response in adult patients with relapsed or refractory acute lymphoblastic leukemia (ALL). A new analysis of data from the ZUMA-3 study shows patients responded to KTE-C19 regardless of prior treatment with blinatumomab, an FDA-approved treatment for relapsed or refractory ALL. After eight or more weeks of follow-up, 63 percent (n=5/8) of patients with prior blinatumomab

treatment and 80 percent (n=8/10) of patients without prior blinatumomab treatment had achieved a complete response or complete response with incomplete hematological recovery. Overall, 94 percent (n=17/18) of patients had minimal residual disease (MRD)-negative remission. KTE-C19 was also manufactured successfully in both groups, with similar product characteristics in terms of CD4/CD8 ratio and other measures.

“As a CD19/CD3 bispecific T cell antibody, the possible impact of prior blinatumomab use on the efficacy of KTE-C19 – a CD19-directed CAR T therapy – was an important question for exploration,” said Bijal Shah, MD, ZUMA-3 investigator and medical oncologist, Moffitt Cancer Center. “We observed that prior blinatumomab use did not affect the manufacturing of efficacious product, and that high response rates were seen regardless of previous treatment with blinatumomab.”

Grade 3 or higher CRS was seen in 27 percent of patients with prior blinatumomab and in 17 percent of patients without prior blinatumomab. Grade 3 or higher neurologic events were seen in 36 percent of patients with prior blinatumomab and 67 percent of patients without prior blinatumomab. A greater number of subjects in the blinatumomab-naïve group received the higher 1×10^6 cells/kg dose.

16. Array BioPharma Announces Additional Median Overall Survival Results of Encorafenib and Binimetinib in Patients with BRAF-mutant Advanced Melanoma

- Combination of encorafenib and binimetinib achieved 33.6 month median overall survival
- Data shows limited use of post-trial immunotherapy across treatment groups
- Phase 3 COLUMBUS results selected for "Best of ASCO"

The results showed median overall survival (mOS) was 33.6 months for patients treated with the combination of encorafenib and binimetinib compared to 16.9 months for patients treated with vemurafenib as a monotherapy. The combination reduced the risk of death compared to treatment with vemurafenib alone [hazard ratio (HR) of 0.61, [95% CI 0.47, 0.79, $p < 0.0001$]. The observed efficacy of vemurafenib in the control arm is also consistent with historical data, providing an additional benchmark for validating the patient population and results observed in COLUMBUS. Further, the two-year OS with combination therapy was 58%.

Importantly, the presentation included data showing limited use of post-trial immunotherapy, which is consistent with other published pivotal trials of BRAF and MEK-inhibitors in *BRAF*-mutant advanced melanoma.

"The data presented today at ASCO demonstrate that the use of subsequent immunotherapies was consistent across treatment groups, indicating that these subsequent treatments are unlikely to have contributed to the observed differences in survival," said Keith T. Flaherty, M.D., Director of the Termeer Center for Targeted Therapy, Massachusetts General Hospital Cancer Center and Professor of Medicine, Harvard Medical School. "This further suggests encorafenib and binimetinib could be a promising new treatment option for patients with *BRAF*-mutant advanced melanoma."

17. Merck's KEYTRUDA® (pembrolizumab) Demonstrated Long-Term Survival Benefit Based on Four and Five Years of Follow-Up from Two Pivotal Studies in Advanced Melanoma

- New Analysis of Four-Year Data for KEYTRUDA from Phase 3 KEYNOTE-006 Study Showed 86 Percent of Patients Were Progression-Free 20 Months After Completing Two Years of KEYTRUDA
- Five-Year Data for KEYTRUDA from Phase 1b KEYNOTE-001 Study Showed Overall Survival Greater Than 40 Percent in Treatment-Naïve Metastatic Melanoma Patients, the Longest Follow-up for KEYTRUDA to Date

A new analysis from KEYNOTE-006 demonstrated durable efficacy benefits among patients who completed two years of KEYTRUDA treatment, combined with updated overall survival (OS) results across both studies, confirming anti-tumor activity in advanced melanoma patients. At a median follow-up of 20.3 months after completion of KEYTRUDA in KEYNOTE-006, 86 percent of patients remained progression-free, the co-primary endpoint for the study. For the primary endpoint of OS in KEYNOTE-006, the four-year OS rate was 41.7 percent in the pooled KEYTRUDA arms vs. 34.1 percent in the ipilimumab arm; in treatment-naïve patients, OS rates were 44.3 percent in the pooled KEYTRUDA arms and 36.4 percent in the ipilimumab arm. In KEYNOTE-001, the five-year OS rate, a secondary endpoint for the study, was 34 percent in all patients and 41 percent in treatment-naïve patients. The safety profile of KEYTRUDA in both studies was consistent with what has been seen in previous trials among patients with advanced melanoma. Results for **KEYNOTE-006** (Abstract #9503) and **KEYNOTE-001** (Abstract #9516) are being presented today at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

“Looking across the findings for both KEYNOTE-006 and KEYNOTE-001 we are seeing further validation that KEYTRUDA is significantly extending the survival of first-line metastatic melanoma patients, regardless of tumor *BRAF*-mutation status,” said Scot Ebbinghaus, M.D., vice president, clinical research, Merck Research Laboratories. “In KEYNOTE-006, we are also seeing durable efficacy benefits for patients who complete two years of KEYTRUDA treatment. We are pleased to share data that further reinforce KEYTRUDA monotherapy as a standard of care in advanced melanoma patients and deliver on our goal of improving and extending the lives of melanoma patients.”

[18. Opdivo \(nivolumab\) 3 mg/kg Demonstrates Sustained, Superior Recurrence-Free Survival Versus Yervoy \(ipilimumab\) 10 mg/kg for Broad Range of Patients with Resected Stage III or IV Melanoma](#)

In the study, *Opdivo* demonstrated superior RFS versus *Yervoy*, regardless of disease stage, PD-L1 expression or *BRAF* mutation status, with RFS rates of 62.6% with *Opdivo* compared to 50.2% with *Yervoy* in the intent-to-treat patient population. In patients with stage IIIB melanoma, RFS rates at 24 months for *Opdivo* were 70.8% versus 60.7% with *Yervoy*; for patients with stage IIIC melanoma, RFS rates were 58.0% with *Opdivo* versus 45.4% with *Yervoy*; and for patients with stage IV melanoma, RFS rates for *Opdivo* were 58.0% versus 44.3% with *Yervoy*. In patients with *BRAF* mutant melanoma, RFS rates for *Opdivo* were 61.9% versus 51.7% with *Yervoy*; in patients with *BRAF* wild-type melanoma, *Opdivo* demonstrated a RFS of 63.5% versus 46.2% with *Yervoy*.

[19. Lynparza in combination with abiraterone delayed disease progression in metastatic castration-resistant prostate cancer](#)

Noel Clarke, Professor of Urological Oncology, Christie NHS Foundation Trust, Manchester, UK, said: “This is the first time we have seen an improvement with the use of a PARP inhibitor in combination

with abiraterone in patients with metastatic castration-resistant prostate cancer and this effect may be independent of HRR status. The data suggest this therapeutic combination may be a promising new treatment approach for this aggressive disease.”

Sean Bohlen, Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca, said: “A previous trial demonstrated improvements in response rates with *Lynparza* monotherapy in metastatic castration-resistant patients with HRR mutations. The Study 08 combination data suggests that regardless of their mutation status, men with metastatic castration-resistant prostate cancer may potentially benefit from *Lynparza* in combination with abiraterone.”

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: “There is a significant unmet medical need for patients with metastatic castration-resistant prostate cancer as they are a high-risk group with limited treatment options. *Lynparza* is the first PARP inhibitor to demonstrate activity in combination with standard-of-care treatment in prostate cancer. These data from Study 08 represent another important milestone in the clinical development of *Lynparza*.”

Median rPFS was 13.8 months with *Lynparza* and abiraterone compared to 8.2 months with abiraterone alone (HR 0.65; 95% CI 0.44-0.97; p=0.034). Median PFS2 was 23.3 months vs 18.5 months (HR 0.79; 95% CI 0.51–1.21). Median OS was 22.7 months with combination treatment versus 20.9 months with abiraterone alone (HR 0.91; 95% CI 0.60–1.38). Pre-specified exploratory subgroup analyses demonstrated an rPFS improvement in patients, regardless of HRR status. Study 08 was not powered for subgroup analyses, PFS2 and OS.

[20. Merck presents updated results from expansion cohorts of the ongoing M7824 Ph I trial \(NCT02517398\) of Bifunctional Immunotherapy M7824](#)

“M7824’s dual approach to fighting cancer, which brings together a TGF- β trap with the anti-PD-L1 mechanism, complements our existing immuno-oncology portfolio,” said Luciano Rossetti, M.D., Global Head of Research & Development at the biopharma business of Merck. “The unique design of this fusion protein offers the potential to optimally engage the TGF- β pathway. This is one example of the creative approaches we are taking to address challenging cancers where we believe we can deliver a transformational change for patients.”

In patients with second line (no prior immunotherapy) advanced NSCLC from the cohort of the ongoing Phase I clinical trial (NCT02517398), signs of clinical activity were seen across PD-L1 expression levels. At the recommended Phase II dose (1200 mg every 2 weeks), an investigator-assessed confirmed overall response rate (ORR) of 40.7% (11/27 patients) was observed in patients with PD-L1+ tumors ($\geq 1\%$, Ab clone 73-10). In patients with high PD-L1+ expressing tumors ($\geq 80\%$; Ab clone 73-10 [$\geq 80\%$ as measured with Ab clone 73-10 comparable with tumor proportion score (TPS) $\geq 50\%$ with 22C3]), ORR was 71.4% (5/7 patients). A median progression-free survival (PFS) of 6.8 months was observed for PD-L1+ patients (1200 mg every 2 weeks) and the median PFS was not reached for the high PD-L1-expressing population owing to the number of patients still responding at the time of analysis. Safety data in this study were consistent with those observed in the overall M7824 Phase I clinical program. The most common treatment-related adverse events (TRAEs) were pruritus (20.0%), maculopapular rash (18.8%) and decreased appetite (12.5%). Grade 3 TRAEs were experienced by 21 patients (26.3%), Grade 4 TRAEs occurred in 2 patients (2.5%). The most common events were skin and subcutaneous tissue disorders. Eight patients (10%) discontinued treatment due to TRAEs.

From the ongoing Phase I, open-label trial NCT03427411 (presented in collaboration with the NCI), signs of tumor burden reduction were seen in 47% (8/17 patients) of patients with advanced HPV associated cancers, including cervical, anal, or head and neck squamous cell carcinoma, enrolled in the dose escalation part of the study. The ORR was 35.3% in patients with HPV associated cancer and 41.7% (including 1 patient with response post-pseudoprogression) in patients with proven HPV-positive disease (12 patients). Safety data in this study were consistent with those observed in the broader M7824 clinical program. A total of 4 patients (23.5%) experienced Grade ≥ 3 TRAEs, including colitis, cystitis, gastroparesis, pleural effusion and hypokalemia (Grade 4); notably, 3 of these patients had tumor burden reduction. No other Grade 4 or 5 TRAEs were seen.

In addition to M7824, data from a number of high-priority clinical development programs are also being presented at ASCO 2018, including tepotinib (NSCLC), M2698 (advanced tumors) and two molecules from the DNA Damage Response portfolio (advanced solid tumors).

21. Preliminary data for NKTR-214 in combination with Nivolumab for patients with stage IV metastatic melanoma, RCC, and urothelial cancers

“In the Phase 1 dose-escalation and Phase 2 expansion stages of the PIVOT trial to-date, we’ve observed important responses, including activity in PD-L1 negative patients,” said Mary Tagliaferri, M.D., Senior Vice President of Clinical Development and Chief Medical Officer at Nektar Therapeutics. “We look forward to advancing this combination into Phase 3.”

Clinical Efficacy (Response measured per RECIST 1.1 for efficacy-evaluable patients (treated at the recommended Phase 2 dose and with ≥ 1 on treatment scan. Response and median time on study calculated from data cut as of May 29, 2018):

- Stage IV Metastatic Treatment-Naïve 1L Melanoma Patients (Enrolled Per Fleming 2-Stage Design at RP2D):
 - Pre-specified efficacy criteria were met for Objective Response Rate (ORR) in Stage 1 (N1=13) with 11/13 (85%) of patients achieving either a partial response (PR) or complete response (CR). Median time on study for 28 patients in Stage 2 (N1+N2) is 4.6 months. Responses were observed in 14/28 (50%) patients (3 CR, 10 PR, 1 uPR). Amongst the 25 patients with known PD-L1 status, ORR in PD-L1 negative patients was 5/12 (42%) and in PD-L1 positive patients was 8/13 (62%). One patient with unknown PD-L1 baseline status experienced a CR.
- Stage IV Metastatic Treatment-Naïve 1L Renal Cell Carcinoma Patients (Enrolled Per Fleming 2-Stage Design at RP2D):
 - Pre-specified efficacy criteria were met for ORR in Stage 1 (N1=11) with 7/11 (64%) of patients achieving a partial response (PR). Median time on study for 26 patients in Stage 2 (N1 + N2) is 5.6 months. Responses were observed in 12/26 (46%) patients (11 PR, 1 uPR). Amongst the 24 patients with known PD-L1 status, The ORR in PD-L1 negative patients was 9/17 (53%) and in PD-L1 positive patients was 2/7 (29%). One of two patients (50%) with unknown PD-L1 baseline status experienced a PR.
- Stage IV Metastatic Treatment-Naïve 1L Urothelial Carcinoma (Enrolled Per Fleming 2-Stage Design at RP2D):

- Pre-specified efficacy criteria were met for ORR in Stage 1 (N1=10) with 6/10 (60%) of patients achieving either a partial or complete response (2 uCR, 3 PR, 1 uPR). Median time on study for 10 patients in Stage 1 is 3.9 months. The ORR in PD-L1 negative patients was 3/5 (60%) and in PD-L1 positive patients was 3/5 (60%).

Biomarkers and Mechanism of Action:

- Data presented show conversion of PD-L1 negative status at baseline to PD-L1 positive status at week 3 in 9/17 patients (53%). Of these previously PD-L1 negative patients, 78% achieved clinical benefit as defined by stable disease, partial response or complete response.

Clinical Safety (Safety database as of May 7, 2018):

- A total of 283 patients have been treated at the RP2D. The most common treatment-related adverse events (TRAEs) were grade 1-2 flu-like symptoms (58.7%), rash (44.5%), fatigue (42.0%), and pruritus (31.4%). A total of 40/283 (14.1%) of patients experienced a Grade 3 (G3) or higher TRAE with 6/283 (2.1%) patients discontinuing treatment due to a TRAE. 10/283 (3.5%) of patients experienced a G3 or higher immune-mediated AE. There was one nivolumab-related G5 pneumonitis reported.

22. Ph II ibrutinib + venetoclax early data show high rates of responses in 1L CLL patients

- Approximately nine out of 10 of the first CLL patients treated achieved responses with no detectable minimal residual disease (MRD) based on a specific test to detect cancer cells in the bone marrow
- Data highlighted in an oral presentation (abstract #7502) and selected for the Best of ASCO Meetings
- Promising data for the combination of ibrutinib and venetoclax suggest the potential for a chemotherapy-free oral regimen for first-line CLL patients

Abstract #7502: Phase 2 CAPTIVATE results of ibrutinib (ibr) plus venetoclax (ven) in first-line chronic lymphocytic leukemia (CLL)

"The findings underscore prior data sets that have been reported by external investigators and support the potential benefit of combining these two agents with complementary mechanisms of action, IMBRUVICA and venetoclax, which may work together to deliver deep responses in chronic lymphocytic leukemia," said Danelle James, M.D., M.A.S., Head of Clinical Science, Pharmacyclics LLC, an AbbVie company. "The Phase 2 results from the CAPTIVATE study suggest we could be one step closer to advancing treatment without the use of chemotherapy for patients with CLL and SLL."

23. Merck's KEYTRUDA® (pembrolizumab) Showed Overall Response Rate of Nearly 40 Percent as First-Line Therapy in Patients with Advanced Clear Cell Renal Cell Carcinoma (RCC) in Phase 2 KEYNOTE-427 Study

Interim data showed an overall response rate (ORR) of 38.2 percent (95% CI, 29.1-47.9) in patients who received KEYTRUDA monotherapy as first-line therapy, the primary endpoint of the study. In a pre-specified, exploratory sub-group analysis based on PD-L1 status, ORR was 50.0 percent (95% CI, 34.9-65.1) in patients whose tumors expressed PD-L1 (CPS \geq 1). In a pre-specified exploratory sub-group analysis based on the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk model, ORR was 42.0 percent (95% CI, 30.2-54.5) in patients with intermediate/poor prognostic risk. This is the first presentation of Phase 2 data for an anti-PD-1 monotherapy as first-line treatment for advanced clear cell RCC. These results, as well as other study findings, are being presented today in an oral session at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #4500).

"Until now, there have been limited data evaluating anti-PD-1 monotherapy in the first-line treatment of advanced clear cell renal cell cancer," said Dr. David F. McDermott, lead study investigator, director, Biologic Therapy and Cutaneous Oncology Programs, Beth Israel Deaconess Medical Center, leader, Dana Farber/Harvard Cancer Center, Kidney Cancer Program, professor of medicine, Harvard Medical School. "With an overall response rate of nearly 40 percent as monotherapy, these data from KEYNOTE-427 are encouraging for clinicians and for patients living with this difficult-to-treat cancer."

24. Results of Phase III RELEVANCE Study Comparing REVLIMID plus Rituximab (R²) Versus Rituximab Plus Chemotherapy in Patients with 1L Follicular Lymphoma

"These findings provide important insight into the efficacy and safety of a chemotherapy-free regimen in patients with previously untreated follicular lymphoma and represent an important step forward in understanding possible treatment options for these patients," said Nathan Fowler, MD, Associate Professor, Department of Lymphoma/Myeloma, University of Texas MD Anderson Cancer Center.

The co-primary efficacy endpoints of the study were CR and CRu at 120 weeks and PFS during the pre-planned analysis (final analysis of CR/CRu and interim analysis of PFS). An analysis of the findings found that 48% of patients in the R² arm and 53% of those receiving R-chemo maintained CR/CRu 120 weeks after randomization, with a 3-year estimated interim PFS rate of 77% and 78% respectively (P=0.48, HR (95% CI) 1.10 (0.85-1.43)). Preliminary overall survival, one of the study's secondary endpoints, showed a 3-year survival rate of 94% in both treatment arms. Other secondary endpoints included number of patients with adverse events, time to treatment failure, event-free survival, time to next anti-lymphoma treatment, time to next chemotherapy treatment, overall response rate at 120 weeks based on International Working Group (IWG) 1999 criteria, and health-related quality of life as measured by the EORTC QLQ-C30.

The majority of patients in both arms completed treatment (69% R² and 71% R-chemo). The most common Grade 3/4 TEAEs in both arms were neutropenia (32% R² vs. 50% R-chemo), febrile neutropenia (2% R² vs. 7% R-chemo) and cutaneous events (7% R² vs. 1% R-chemo). SPMs were reported in 7% R² and 10% R-chemo patients, and Grade 5 AEs were 1% in both treatment arms.

25. Third Novartis Phase III trial shows Kisqali® combination therapy significantly improves PFS in HR+/HER2- advanced breast cancer

- Kisqali plus fulvestrant demonstrated superior efficacy, with a median PFS of 20.5 months vs. 12.8 months for fulvestrant alone, among overall study population of first- and second-line postmenopausal patients with HR+/HER2- advanced breast cancer
- In the subgroup of patients taking Kisqali plus fulvestrant in the first-line setting, median PFS was not reached and 70% were estimated to remain progression-free at median follow-up of 16.5 months
- MONALEESA-3 is the only randomized Phase III trial to study a CDK4/6 inhibitor plus fulvestrant in the first-line setting showing efficacy in patients with de novo advanced breast cancer and those who had not received adjuvant therapy in more than a year

"The MONALEESA-3 results in patients treated in this first-line setting were particularly significant. Nearly 70% of women who received ribociclib plus fulvestrant in this setting were estimated to remain progression-free at the median follow-up of 16.5 months," said Dennis J. Slamon, MD, Director of Clinical/Translational Research, University of California, Los Angeles Jonsson Comprehensive Cancer Center. "In the advanced breast cancer setting, it is important to ensure we provide patients with treatment options that increase time to disease progression while also maintaining quality of life."

26. Updated ALEX trial results show alectinib further outpacing crizotinib in treatment naive ALK+ NSCLC

Updated results of the global phase III ALEX trial comparing alectinib with crizotinib as first-line treatment against ALK-positive non-small cell lung cancer show a median progression-free survival (PFS) of 34.8 months in 152 patients treated with alectinib versus 10.9 months in 151 patients treated with crizotinib.

"Think of it like a horse race, only it's not about who crosses the finish line first, but how far the horses can run," says D. Ross Camidge, MD, PhD, the Joyce Zeff Chair in Lung Cancer Research at the University of Colorado Cancer Center, director of Thoracic Oncology at the CU School of Medicine, and the study's first author. "In this trial, it's as if half of the people 'riding' crizotinib had exhausted their horses at about 11 months. For patients on alectinib, when this trial first started reporting data last year, more than half were still on their horses, still running. Now enough time has elapsed to estimate the median performance of these alectinib 'horses' more accurately."

Camidge's analogy explains the results above: At 10.9 months half of the cancers treated with crizotinib had restarted their growth, whereas it took 34.8 months for patients on alectinib to reach this same "median progression free survival". Impressively, the PFS was almost identical in patients without brain metastases at the point of diagnosis, demonstrating the drug's success broad overall cancer control.

Additionally, 45 percent of patients treated with crizotinib went on to develop brain metastases while on trial, compared with only 12 percent of patients treated with alectinib. The overall response rate for alectinib was 82.9 percent, compared with 75.5 percent for crizotinib. And alectinib was also associated with fewer overall side effects than crizotinib, with 16 percent of alectinib patients requiring dose reduction and 22 percent requiring dose interruption, compared with 21 and 25 percent of crizotinib patients, respectively.

27. KEYTRUDA® (pembrolizumab) Monotherapy Significantly Improved Overall Survival in KEYNOTE-042 Study as First-Line Treatment for Locally Advanced or Metastatic NSCLC Patients Whose Tumors Expressed PD-L1 (TPS ≥1%)

- Study Results Confirm KEYTRUDA is the Only Anti-PD-1 Therapy to Show an Overall Survival Benefit as Monotherapy in First-Line NSCLC

In this study, KEYTRUDA monotherapy resulted in significantly longer overall survival (OS) than platinum-based chemotherapy (carboplatin plus paclitaxel or carboplatin plus pemetrexed) in patients with a PD-L1 tumor proportion score (TPS) of ≥1 percent. As part of a pre-specified analysis plan, OS was sequentially tested and was significantly improved in patients with a TPS of ≥50 percent (HR=0.69 [95% CI, 0.56-0.85]; p=0.0003), with a TPS of ≥20 percent (HR=0.77 [95% CI, 0.64-0.92]; p=0.0020), and then in the entire study population with a TPS of ≥1 percent (HR=0.81 [95% CI, 0.71-0.93]; p=0.0018). These results will be presented today in the plenary session and during the Sunday press program at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #LBA4).

“In the entire KEYNOTE-042 study population of patients expressing PD-L1 in at least 1 percent of tumor cells, first-line treatment with KEYTRUDA as monotherapy significantly improved overall survival in patients with either locally advanced or metastatic non-small cell lung cancer across histologies,” said Dr. Gilberto Lopes, study investigator and associate director for global oncology at the Sylvester Comprehensive Cancer Center at the University of Miami. “As a clinician treating patients with advanced lung cancer every day, it is encouraging to have additional data on KEYTRUDA’s benefits on overall survival, the primary goal of therapy for patients newly diagnosed with this deadly disease.”

28. Erdafitinib shows promise in urothelial cancer patients with specific mutations

In an international Phase II trial led by researchers at The University of Texas MD Anderson Cancer Center, treatment with the oral FGFR inhibitor erdafitinib (ERDA) was well-tolerated and achieved a robust response for patients with metastatic urothelial, or urinary tract, cancers harboring mutations in the FGFR3 gene.

The targeted therapy also appeared effective in a subset of patients for whom immunotherapy had previously failed, suggesting ERDA may provide benefit for patients without further treatment options. The results, presented at the 2018 American Society of Clinical Oncology Annual Meeting by principal investigator Arlene Siefker-Radtke, M.D., professor of Genitourinary Medical Oncology, also were granted the “Best of ASCO” designation.

“Given the limited treatment options for urothelial cancer, we still have a long way to go to benefit our patients. Having a therapy with a response rate around 40 percent, with the convenience of being an oral medication, certainly fits an unmet need,” said Siefker-Radtke.

29. Exelixis Announces Results from Sub-Group Analyses of the Phase 3 Pivotal CELESTIAL Trial of Cabozantinib for Advanced HCC

The sub-analysis of patients in CELESTIAL who received sorafenib as their only prior systemic therapy was presented by Robin Kate Kelley, M.D., University of California San Francisco. In this subgroup-analysis, patients were grouped by the length of time they had been treated with sorafenib (less than three months; three to six months; more than six months) to assess the effect of cabozantinib in patients with varying benefit from prior sorafenib. In all three groups, cabozantinib improved OS and PFS versus placebo.

“We’re pleased with the encouraging CELESTIAL subgroup data presented at ASCO, which showed that cabozantinib provided benefits to patients regardless of duration of prior sorafenib treatment or age,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “We continue to work closely with the U.S. FDA as they review the filing application for cabozantinib for previously treated advanced hepatocellular carcinoma and hope it may soon provide a new option for patients with this difficult-to-treat cancer who have few alternatives.”

30. Immunomedics Reveals Promising Data for Sacituzumab Govitecan in Patients Heavily Pretreated for Metastatic Estrogen Receptor-Positive Breast Cancer

“Sacituzumab govitecan has demonstrated encouraging activity in heavily pretreated patients with a median of five prior treatment lines for metastatic disease,” said Aditya Bardia, MD, MPH, Director of Precision Medicine and attending physician at Center for Breast Cancer, Massachusetts General Hospital, Harvard Medical School, Boston, MA, who presented the study in an oral session on Sunday, June 3, 2018 at the ASCO Annual Meeting. “Women with ER+/HER2– mBC who have progressed on endocrine therapies and initial chemotherapy, have very limited treatment options, and sacituzumab govitecan, based on the results presented today, could provide a promising option.”

In the Phase 1/2 study, 54 patients with ER+/HER2– mBC who received sacituzumab govitecan at a dose of 10 mg/kg on days 1 and 8 of three-week cycles showed a confirmed overall response rate (ORR) of 31 percent (17/54), based on local investigator assessment in accordance with RECIST 1.1. The estimated median duration of response was 7.4 months (95% CI: 4.4, 18.3), the clinical benefit rate (CBR; partial response and stable disease lasting for six months and longer) was 48 percent (26/54). At the time of data cutoff on April 30, 2018, seven responders were still receiving sacituzumab govitecan.

In the subgroup of 37 patients who also had received prior CDK 4/6 inhibitors, ORR was 24 percent (9/37). In the difficult-to-treat subgroup of patients with liver metastases, CBR was 48 percent (21/44). The estimated median progression-free survival was 6.8 months (95% CI: 4.6, 8.9).

31. IMV Inc. (Formerly Immunovaccine Inc.) Presents New Positive Data From Phase 1b/2 Combination Clinical Trial in Advanced Ovarian Cancer

- Combination Immunotherapy Continues to Show Tolerable Safety Profile and Promising Activity With Second Dosing Cohort Showing 6 of the First 8 Evaluable Participants Exhibiting Stable Disease at First CT Scan

- Tumor Analyses From First Dosing Cohort Demonstrates DPX-Survivac's Mechanism of Action; Establishes First Clinical Demonstration of a Correlation Between Partial Tumor Regressions and Tumor T Cell Infiltration

At the time of data cut-off, 39 patients were enrolled (including 25 new participants in the 300mg cohort with 8 evaluable from day 56 first CT scan). Data from the first 18 evaluable patients across both dosing cohorts showed:

- 7 tumor regressions, including 4 Partial Responses (PR) reported so far (PR, defined as $\geq 30\%$ decrease in tumor lesion size);
- Study participants were generally tolerating treatments well, with no related significant adverse events (SAEs) reported.
- Data from the first 8 evaluable participants in the 300mg epacadostat dosing cohort at first CT scan included:
- 6 patients demonstrated stable disease (SD) at day 56, with 4 of these SDs still on trial at data cut-off;
- 2 patients with tumor regressions observed so far, including one PR with a tumor regression ongoing for more than 9 months.

IMV plans to report updated results on these patients and others enrolled in the trial when data from at least 16 evaluable participants in the second dosing cohort are available.

Researchers also analyzed patient data to study the combination's mechanism of action (MOA). They examined blood samples and tumor biopsies for the 10 evaluable patients treated in the first dosing cohort. These data showed:

- Survivin-specific T cell responses detected in 100% (10/10) of patients
- Increase in T cell infiltration post treatment in 37% (3/8) of the analyzable tumor biopsies based on two complementary testing methodologies (RNA sequencing and immunohistochemistry)
- 2 of the 3 patients with T cell infiltration showed PRs with significant and durable tumor regressions lasting more than one year.
- The third patient with T cell infiltration exhibited Progressive Disease (PD) with evidence of down regulation of the major histocompatibility (MHC) presentation pathway and significant increases in suppressive markers, both indicative of mechanisms of resistance.

32. Merck presents update on Tepotinib in advanced lung cancer

- *Data from an ongoing Phase II tepotinib study show anti-tumor clinical activity in patients with advanced non-small cell lung cancer harboring MET exon 14 skipping mutations*
- *Patients with advanced lung cancer harboring MET exon 14 mutations currently have a poor prognosis and limited treatment options*
- *Safety data are consistent with data previously reported, with no new safety signals identified*

"Patients living with advanced non-small cell lung cancer harboring *MET* exon 14 skipping mutations have limited treatment options available to them and typically face poor clinical outcomes," said investigator Enriqueta Felip, M.D., Medical Oncologist, Vall d'Hebron Institute of Oncology (VHIO). "More than half of the patients in the Phase II VISION study had an investigator-

assessed confirmed response, demonstrating the potential of tepotinib and the need to further evaluate this precision medicine option."

Initial data from the Phase II VISION study of tepotinib in patients living with advanced NSCLC harboring *MET* exon 14 skipping mutations will be presented today at ASCO during the "Lung Cancer-Non-Small Cell Metastatic" poster discussion session, 11:30 a.m. - 12:45 p.m. CDT. Treatment with tepotinib led to a confirmed complete response (CR) or confirmed partial response (PR) in 53.6% (15/28) and stable disease (SD) in 17.9% (5/28) of patients based on investigator assessment. Based on independent assessment of updated data from 28 patients (patients with at least 2 post-baseline assessments or who discontinued for any reason), 42.9% (12/28) had a PR and 21.4% (6/28) had SD.

33. Nivolumab + chemotherapy show improved PFS in 1L squamous and non-sq. NSCLC patients with PD-L1 <1% in CheckMate-227 study

Data show that *Opdivo* plus chemotherapy (n=177) extended progression-free survival (PFS) versus chemotherapy (n=186) in patients with PD-L1 expression <1% (HR 0.74; 95% CI: 0.58 to 0.94). PFS is a secondary endpoint for *Opdivo* plus chemotherapy in Part 1b of the study, and results are based on a descriptive analysis.

In an exploratory analysis of patients with high tumor mutational burden (TMB) ≥ 10 mutations/megabase (mut/Mb) and PD-L1 expression <1%, the one-year PFS rates were 45% with *Opdivo* plus low-dose *Yervoy* (n=38), 27% with *Opdivo* plus chemotherapy (n=43) and 8% with chemotherapy (n=48). In patients with low TMB (<10 mut/Mb) and PD-L1 <1%, the one-year PFS rate was 18% with both *Opdivo* plus low-dose *Yervoy* (n=52) and *Opdivo* plus chemotherapy (n=54) and was 16% with chemotherapy (n=59).

Hossein Borghaei, D.O., study investigator and chief of thoracic medical oncology at Fox Chase Cancer Center in Philadelphia, said, "For the first time, CheckMate -227 allows the oncology community to look at I-O/I-O and I-O/chemotherapy in one data set. Results show *Opdivo* plus chemotherapy improved progression-free survival versus chemotherapy in first-line lung cancer patients whose tumors do not express PD-L1. Taken together with the totality of CheckMate -227 data presented to date, the results reinforce that TMB status provides clinically relevant information for *Opdivo*-based combinations and that *Opdivo* plus low-dose *Yervoy* provided durable efficacy in patients with high TMB."

34. Two Year Update of Pivotal JAVELIN Merkel 200 Trial Shows Continued Durable Responses with Avelumab in MCC

In JAVELIN Merkel 200 – an open-label, single-arm Phase II study – patients with histologically confirmed mMCC whose disease had progressed on or after chemotherapy administered for distant metastatic disease received BAVENCIO 10 mg/kg intravenously every two weeks until disease progression or unacceptable toxicity. Eighty-eight patients were followed for a median of 29.2 months (range 24.8–38.1 months). The confirmed overall response rate (ORR) of 33% (95% confidence interval [CI] 23.3–43.8; complete response in 11.4%) remained unchanged from previous analyses reported at both one year and 18 months. Responses remained ongoing in 19 of 29 patients who responded to treatment, including 12 patients whose duration of response exceeded two years.

Durable responses led to stable rates of PFS (29% at 12 months, 29% at 18 months and 26% at 24 months). Median OS was 12.6 months (95% CI 7.5–17.1) and the two-year OS rate was 36% (50% at 12 months and 39% at 18 months). With a minimum follow-up of two years, no new safety signals were identified for BAVENCIO and was consistent with prior reports. Sixty-seven patients (76.1%) had a treatment related adverse event (TRAE), 10 patients (11.4%) had a Grade 3 or less TRAE and 20 patients (22.7%) had an immune-related adverse event. No treatment-related deaths occurred.

“These results represent a key milestone for patients with mMCC, as chemotherapy has historically been the only treatment option for this devastating disease,” said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-Oncology, Early Development and Translational Oncology, Pfizer Global Product Development. “These data, alongside the additional real-world data which are also being presented at ASCO, strengthen our confidence in BAVENCIO as a treatment option for this rare and aggressive skin cancer.”

[35. Celgene announces updated safety and efficacy data from the TRANSCEND trial of liso-cel \(JCAR017\) in patients with R/R B-cell non-Hodgkin Lymphoma](#)

"As liso-cel data mature, the durable response rates continue to demonstrate the potential of CAR T cell therapy in patients with DLBCL who have relapsed or are refractory to prior treatments," said principal investigator Jeremy Abramson, M.D., of Massachusetts General Hospital. "Added to the emerging side effect profile with liso-cel, this therapy has encouraging potential in diffuse large B-cell lymphoma."

At six months, 49% of patients remained in remission, with 46% maintaining a complete response (CR) in this cohort (n=37). When durability of response beyond six months was evaluated across all dosing levels ranging from 5×10^7 to 1×10^8 CAR T cells, 93% of patients in CR remained in CR at data cut off. Liso-cel therapy was available for 99% (132/134) of patients apheresed.

The most common treatment-emergent adverse events that occurred at $\geq 25\%$ incidence included neutropenia (63%), anemia (53%), fatigue (46%), thrombocytopenia (34%), decreased appetite (29%), nausea (28%), hypotension (26%), cough (26%), headache (25%), dizziness (25%), constipation (25%), and diarrhea (25%). Cytokine release syndrome and neurotoxicity were observed at a rate of 37% and 23% for all grades, and 1% and 13% for grades 3 and 4, respectively (n=102). Based on this emerging safety profile, outpatient administration is being evaluated in the TRANSCEND trial.

[36. Roche presents new data across a range of blood cancers](#)

- Further data demonstrate polatuzumab vedotin’s clinical efficacy across a range of diffuse large B-cell lymphoma subgroups
- Additional results from the randomised phase III MURANO study support fixed-duration Venclexta/Venclyxto plus MabThera/Rituxan as a new chemotherapy-free treatment option in previously treated chronic lymphocytic leukaemia
- Updated data highlight Venclexta/Venclyxto’s potential in previously untreated acute myeloid leukaemia

“We’re excited to be presenting a range of data highlighting potential advances in different blood cancers at ASCO this year,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of

Global Product Development. "Roche is committed to bringing practice changing treatments to people with blood cancer through its large and broad development programmes in haematology".

37. anti-BCMA CAR T-cell therapy bb2121 adds nearly 1 year of PFS for heavily pretreated relapsed/refractory multiple myeloma in Ph I CRB-401 trial

Overall response rate in the 18 evaluable pts in DE cohorts $\geq 150 \times 10^6$ CAR T cells was 94%; 10 of 18 (56%) pts had CR or unconfirmed CR; 9 of 10 evaluable pts were MRD-negative. With a median follow-up of 40 weeks in $\geq 150 \times 10^6$ DE cohorts, median response duration and progression-free survival (PFS) had not been reached; PFS rates at 6 and 9 months were 81% and 71%, respectively. Doses of 150 to 300×10^6 CAR T cells were selected for the Exp phase.

38. Pomalidomide triplet (Pomalidomide, bortezomib, and low-dose dexamethasone) extends PFS in relapsed/refractory lenalidomide-exposed myeloma patients in Ph III OPTIMISMM trial

After a median follow-up of 16 mos, Pvd significantly reduced the risk of progression or death by 39% vs Vd. OS data are not mature. Most common grade 3/4 treatment-emergent AEs were neutropenia (42% vs 9%), infections (31% vs 18%), and thrombocytopenia (27% vs 29%).

"The results of the OPTIMISMM trial continue to bolster the growing body of research into combination regimens based on the foundation of our IMiD[®] therapies," said Nadim Ahmed, President of Hematology and Oncology for Celgene. "We are excited by the findings, as they illustrate the potential for a pomalidomide-based triplet regimen to be used earlier in the treatment course. The study also included patients who received Pvd immediately following progression after lenalidomide treatment, a growing and clinically relevant patient population for which no phase III data were available until now."

39. Venetoclax/Carfilzomib combo highly effective for t(11;14) R/R myeloma

Of 17 pts evaluated after completing ≥ 2 cycles, 3 had CRs, 2 VGPRs, 3 PRs, 3 SDs, and 2 PD (awaiting response data for 4 pts). Median time to first response was 1 month. Of 5 evaluable pts with t(11;14) MM, 1 achieved CR, 1 VGPR, 3 PR. 85% of pts had an AE, grade 3/4 AEs were neutropenia (15%), hypertension (12%), thrombocytopenia (8%), decreased white blood cells (8%), and nausea (4%). 7 serious AEs occurred, but no dose-limiting toxicities were reported.

40. Boston Biomedical, Inc. highlights presentations on investigational agents napabucasin and DSP-7888 (ombipepimut-S*)

On June 3, updated data from a ph Ib/II trial evaluating napabucasin in combination with nab-paclitaxel and gemcitabine in patients with metastatic pancreatic adenocarcinoma (mPDAC) was presented (abstract #4110, [NCT02231723](#)). Trial results to date showed napabucasin was generally well-tolerated when combined with nab-paclitaxel and gemcitabine, with the majority of TRAEs being gastrointestinal in nature, mainly Gr 1 or 2, and manageable with supportive medication.

Secondary measures showed that nababucasin in combination with nab-paclitaxel and gemcitabine showed signs of clinical activity in patients with mPDAC, with DCR observed in 46 of 59 patients (78%), including two CRs (3%) and 26 PRs (44%) among the 50 patients evaluable by RECIST criteria. Secondary endpoints also showed a maturing mPFS of 7.06 months (95% CI: 5.68, 9.00) and mOS of 9.59 months (8.11, 13.50).

"Pancreatic cancer continues to be one of the most difficult to treat cancers, and new innovative treatments are urgently needed for these patients," said Tanios S. Bekaii-Saab, M.D., FACP, lead author and presenter of the company's phase 1b/2 data and co-leader of the GI Cancer Program at Mayo Clinic Cancer Center. "Building off data that was shared last year, these encouraging findings demonstrate the potential of combining nababucasin with chemotherapy to improve patient outcomes in pancreatic cancer."

[41. Daiichi Sankyo presents long-term Ph I results of DS-8201 in patients with HER2-expressing breast, gastric and other solid cancers](#)

Updated subgroup analysis in 34 heavily pretreated patients with HER2-low-expressing metastatic breast cancer demonstrated a 50.0% confirmed ORR and an 85.3% DCR with DS-8201.

A 54.5% confirmed ORR and a 93.9% DCR was demonstrated with DS-8201 in updated subgroup analysis of patients with HER2-positive metastatic breast cancer pretreated with ado-trastuzumab emtansine (T-DM1) (as well as trastuzumab and pertuzumab in the majority of cases).

Confirmed responses and disease control also were observed with investigational DS-8201 in HER2-expressing gastric cancer and other solid tumors including colorectal and non-small cell lung cancer.

Broad and comprehensive program is underway to accelerate development of DS-8201 including two pivotal phase II trials in metastatic breast cancer (DESTINY-Breast01) and gastric cancer (DESTINY-Gastric01) with plans proceeding to initiate phase III studies in HER2-positive and HER2-low-expressing metastatic breast cancer.

[42. Abstract describing use of Oregovomab in Pancreatic Cancer to be published in JCO](#)

This proof-of-concept open label study recruited a total of 11 patients, 9 of whom received oregovomab immunization. Five patients received five cycles of oregovomab chemoimmunotherapy ("CIT") and four patients received seven cycles of CIT. All nine received stereotactic radiotherapy following their cycles of CIT. Out of the four patients receiving seven cycles of CIT, two patients developed CA125-specific IFN γ positive CD8 T cell response and survived over 28 months and 31 months, respectively, compared to a median survival of 13 months in the study. The results also showed that previously demonstrated immune response associated with CIT was not negatively impacted by use of radiotherapy.

"The data continues to support that oregovomab CIT can induce antigen specific T-cell responses in cancer patients that translate into clinical benefits. It also provides further evidence that our antibody based immunotherapy is a platform technology that can be used with different cancers that express the same cancer antigen," commented Dr. Madiyalakan, CEO of OncoQuest. "We are also continuing our study of oregovomab in both front line and recurrent ovarian cancer to identify

combinations which result in demonstrable clinical benefit and will provide the basis for moving this promising treatment forward to registration."

43. Study design of CD205-Shuttle, a first-in-human trial of MEN1309/OBT076 presented

A multicenter first-in-human clinical study to evaluate MEN1309/OBT076, an antibody drug conjugate (ADC) investigated for the treatment of metastatic solid tumors and non-Hodgkin's lymphoma (NHL) was presented.

MEN1309/OBT076 is a fully humanized IgG1 monoclonal antibody, in co-development with Oxford BioTherapeutics (OBT), conjugated to a potent cytotoxic maytansinoid toxin via a cleavable linker. The ADC is directed against a type I transmembrane glycoprotein CD205/Ly75, that is over-expressed in several solid tumors and NHL.

The **CD205-Shuttle study** is ongoing in major European oncology centers in Italy, Spain, Belgium and the UK. The study investigated to date 5 dose levels. The sixth dose level is currently being evaluated.

44. Agios presents data from Ph I dose-escalation study of AG-881 in patients with IDH mutant positive advanced glioma and other solid tumors

"IDH mutant glioma is a distinct disease where patients are typically diagnosed in their thirties and forties and endure a deteriorating quality of life from the side effects associated with multiple rounds of surgery, radiation and chemotherapy and ultimately die of their disease," said Ingo Mellinghoff, M.D., Memorial Sloan Kettering Cancer Center, an investigator for the study. "The AG-881 Phase 1 dose-escalation data are encouraging, as they demonstrate a favorable safety profile at lower dose levels and show signals of clinical activity that support further evaluation of the role of inhibiting mutant IDH in low-grade glioma."

"With no curative or approved targeted therapies for low-grade glioma and a poor long-term prognosis, we are committed to exploring the novel mechanism of action of our IDH inhibitors in this indication," said Chris Bowden, M.D., chief medical officer at Agios. "Data from our ivosidenib and AG-881 Phase 1 trials and the ongoing perioperative study, combined with feedback from regulators and the neurology community, will inform our pivotal development plan."

45. Updated data from Ivosidenib Ph I dose-escalation and expansion trial in IDH1m relapsed or refractory AML continue to show durable responses as a single agent

- In 179 Relapsed or Refractory IDH1m AML Patients, Primary Endpoint of CR+CRh Rate of 31.8% with a Median Duration CR+CRh of 8.2 Months
- Updated Data Suggest that R/R AML Patients with IDH1-Mutation Clearance Who Have Achieved CR/CRh Have Prolonged Duration of Remission and Overall Survival
- Ivosidenib Phase 1 Data in Patients with IDH1m Advanced Hematological Malignancies Published Today in the New England Journal of Medicine

“The findings presented at ASCO demonstrate that single agent ivosidenib induced durable responses, in some cases with IDH1-mutation clearance, and led to favorable responses compared with historical patient outcomes in a high-risk, molecularly-defined R/R AML population,” said Daniel Pollyea, M.D., M.S., study investigator and clinical director of leukemia services at the University of Colorado School of Medicine. “Additional clinical benefits included transfusion independence and, in responding patients, reductions in advanced-grade infections and febrile neutropenia, indicating immune system recovery with functional neutrophils.”

“These data provide additional clinical and translational observations beyond the 2017 ASH presentation, including preliminary data suggesting that R/R AML patients with IDH1-mutation clearance in bone marrow who have achieved CR/CRh have prolonged remission durations and overall survival versus those without IDH1-mutation clearance,” said Chris Bowden, M.D., chief medical officer of Agios. “We believe the compelling single-agent efficacy coupled with a tolerable safety profile validate the potential for ivosidenib to be a first-in-class therapy for patients with R/R AML and an IDH1 mutation.”

[46. Jounce Therapeutics presents preliminary efficacy data from ongoing Ph I/II ICONIC trial of JTX-2011 in patients with advanced cancers](#)

Safety

- JTX-2011 was well tolerated alone and in combination with nivolumab 240 mg every 3 weeks. The overall safety profile observed was consistent with previously reported data from the Phase 1 portion of the ICONIC trial.

Clinical Activity

Gastric Cancer

- A RECIST partial response (PR) with JTX-2011 monotherapy was observed in 1 of 8 Phase 2 patients (7 PD-1 inhibitor naïve, including PR), ongoing at 8.5+ months.
- Two RECIST PRs with JTX-2011 plus nivolumab were observed in 1 of 4 Phase 1 patients (all PD-1 inhibitor naïve) and 1 of 28 Phase 2 patients (22 PD-1 inhibitor naïve, including PR), ongoing at 11+ and 4+ months, respectively.
- Disease control was observed in 10 of 28 and tumor reductions were observed in 8 of 28 Phase 2 patients treated with JTX-2011 plus nivolumab, including both PD-1 inhibitor naïve and PD-1 inhibitor failures.

Triple Negative Breast Cancer (TNBC)

- A RECIST PR with JTX-2011 plus nivolumab was observed in 1 of 17 Ph II patients (16 PD-1 inhibitor naïve, including PR), ongoing at 4+ months.
- Disease control was observed in 3 of 17 and tumor reductions were observed in 2 of 17 Ph II patients treated with JTX-2011 plus nivolumab, all PD-1 inhibitor naïve.

Head and neck squamous cell cancer (HNSCC) PD-1 inhibitor failures

- Disease control was observed in 2 of 16 and tumor reductions were observed in 1 of 16 Ph II patients treated with JTX-2011 plus nivolumab, all PD-1 inhibitor failures, of whom over 50% were refractory to prior PD-1 inhibitors.

Non-small cell lung cancer (NSCLC) PD-1 inhibitor failures

- Disease control was observed in 7 of 12 and tumor reductions were observed in 4 of 12 Phase 2 patients treated with JTX-2011 plus nivolumab, all PD-1 inhibitor failures.

(1) Disease control= confirmed PR + SD ≥ 9 weeks

(2) Refractory= best response to prior PD-1 inhibitor was progressive disease

47. Moxetumomab pasudotox pivotal data in patients with previously-treated hairy cell leukemia presented

Moxetumomab pasudotox, an investigational anti-CD22 recombinant immunotoxin, showed a 75% objective response (OR) rate, a 41% complete response (CR) rate, and a 30% durable CR rate (primary endpoint). The majority of patients with a complete response had a durable response (73%; 24/33) and achieved a negative minimal residual disease (MRD) status (82%; 27/33). Findings from this pivotal trial were presented for the first time during an oral session at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

Sean Bohan, Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca, said: “Moxetumomab pasudotox is an investigational, first-in-class immunotoxin which we believe has the potential to advance outcomes for patients with relapsed or refractory hairy cell leukemia, a condition with a high unmet need. It is also the first agent to be submitted for regulatory review from our Antibody Drug Conjugates platform, and as such demonstrates our commitment to developing novel treatments for blood cancer.”

48. Long-term IMPACT data find improved survival when targeted therapies matched to tumor-specific gene mutations

All 3,743 patients enrolled in IMPACT received molecular testing; 1,307 were found to have at least one molecular alteration, with 711 receiving MTT (with or without chemotherapy) and 596 receiving NMT. The majority of IMPACT participants who received MTT received an investigational drug then being tested in a clinical trial; others received an FDA-approved targeted therapy commercially approved for another indication.

In those who received MTT, the median PFS was 4 months and the median OS was 9.3 months, compared to 2.8 months and 7.3 months, respectively, in those who received NMT.

“When we opened IMPACT, it was viewed as incredibly novel. Because of the variability, frequency and rarity of alterations in specific solid tumor types, it was thought it would be difficult to use molecular testing for clinical trial selection, without taking into consideration any specific characteristics,” Tsimberidou said. “However, gleaned from our Gleevec-CML experience, we hypothesized that genetic and molecular analysis of solid tumors also could enable the selection of optimal therapy for patients with solid tumors.”

[49. Taselisib and fulvestrant combination slows growth of most common type of advanced breast cancer in SANDPIPER trial](#)

The SANDPIPER study confirms the clinical activity in this selected population. The study met its primary endpoint showing a two-month improvement of median progression-free survival, equating to a 30 percent risk reduction of disease progression (5.4 months with fulvestrant and placebo versus 7.4 months with taselisib and fulvestrant). The response rate more than doubled when taselisib was added to treatment (11.9 percent versus 28 percent). Overall survival data are not yet mature. The safety profile of the combination was associated with considerable toxicities thought to be associated linked to the targeting of the PI3K pathway. The most common side effects included diarrhea, high blood pressure, and colitis. Seventeen percent of individuals who received taselisib stopped treatment early due to side effects.

“We have showed that taselisib improves benefit from fulvestrant in this population by 30 percent,” explained Dr. Baselga, the study’s lead author. “This work confirms the benefit of targeting the PI3K pathway and represents a significant step forward in developing a new class of agents for breast cancer. While there is more work to be done to diminish the side effects and toxicity, I am encouraged by these results.”

[50. Loxo Oncology announces positive interim clinical data from LOXO-292 dose escalation Ph I LIBRETTO-001 trial in RET-altered cancers](#)

- 77% ORR in RET Fusion Cancers and 45% ORR in RET Mutated Medullary Thyroid Cancer (MTC)
- Activity Observed Independent of RET Alteration, Tumor Type (Lung, Thyroid, Pancreas), or Prior Multikinase Inhibitor (MKI) Treatment

“The LOXO-292 Phase 1 data are striking,” said Alexander Drilon, M.D., clinical director in the Early Drug Development Service at Memorial Sloan Kettering Cancer Center and presenting author. “The activity we reported is impressive and I am thrilled to see this promising efficacy with limited adverse events, especially in this heavily pre-treated patient population of RET fusion cancers, including those with brain metastases, and RET mutated MTC.”

“We are very excited to share the initial LOXO-292 clinical experience with the oncology community at ASCO,” said Josh Bilenker, M.D., chief executive officer of Loxo Oncology. “We have long believed that patients with RET fusion cancers and RET mutated MTC needed a purpose-built medicine tailored to their tumors. We hope that LOXO-292 continues to deliver on that premise. Thank you to the patients, investigators and clinical trial teams who made possible today’s presentation.”

[51. New Novartis data found nearly half of CML patients treated with Nilotinib remain in remission almost three years after stopping therapy](#)

- ENESTop and ENESTfreedom data evaluate Treatment-free Remission (TFR) rates at 144 weeks among eligible Ph+ CML-CP patients who stopped Tasigna®

- Findings further support durability and safety of TFR with Tassigna; nearly all patients who lost TFR regained major molecular response after restarting therapy
- Novartis commitment to seek new solutions in CML continues with update of Phase III trial evaluating asciminib, an investigational BCR-ABL1 inhibitor

"Treatment-free Remission is a new treatment goal in CML," said François-Xavier Mahon, Cancer Center of Bordeaux, Institut Bergonié and lead investigator of ENESTop. "Clinical studies like ENESTop and ENESTfreedom offer evidence that when a Ph+ CML-CP patient achieves a deep molecular response with Tassigna, along with other eligibility criteria, s/he can attempt TFR and have a nearly 50% chance of remaining treatment-free long-term. These results confirm an exciting opportunity for eligible patients - the opportunity to reduce time on drug for a chronic leukemia."

52. Astellas and Seattle Genetics present Enfortumab Vedotin data in patients with locally advanced or metastatic Urothelial Cancer previously treated with checkpoint inhibitor therapy

- Of 112 evaluable patients, confirmed complete responses were observed in 4 patients and confirmed partial responses were observed in 41 patients, with an overall response rate of 41 percent.
- The most commonly reported treatment-related adverse event was All Grade fatigue (54 percent). Anemia (8 percent), hyponatremia (7 percent), urinary tract infection (7 percent) and hyperglycemia (6 percent) were the most common \geq Grade 3 AEs.¹ Four patients experienced a fatal treatment-related adverse event (respiratory failure, urinary tract obstruction, diabetic ketoacidosis, multi-organ failure).
- Additionally, the ORR in the 89 patients with prior checkpoint inhibitor therapy was 40 percent, 44 percent in the 23 patients who had not been treated with a checkpoint inhibitor, and 39 percent in the 33 patients with liver metastases.

For all enrolled patients, the interim mOS was 13.6 months, the overall mDOR was 5.75 months and the mPFS was 5.4 months.

"We are encouraged by these updated data for enfortumab vedotin, which further support the rapid expansion of a comprehensive clinical trial program and the registrational study that is already underway in metastatic urothelial cancer," said Steven Benner, M.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development, Astellas. "We look forward to working closely with our partner, Seattle Genetics, as we continue to evaluate enfortumab vedotin for patients with metastatic urothelial cancer."