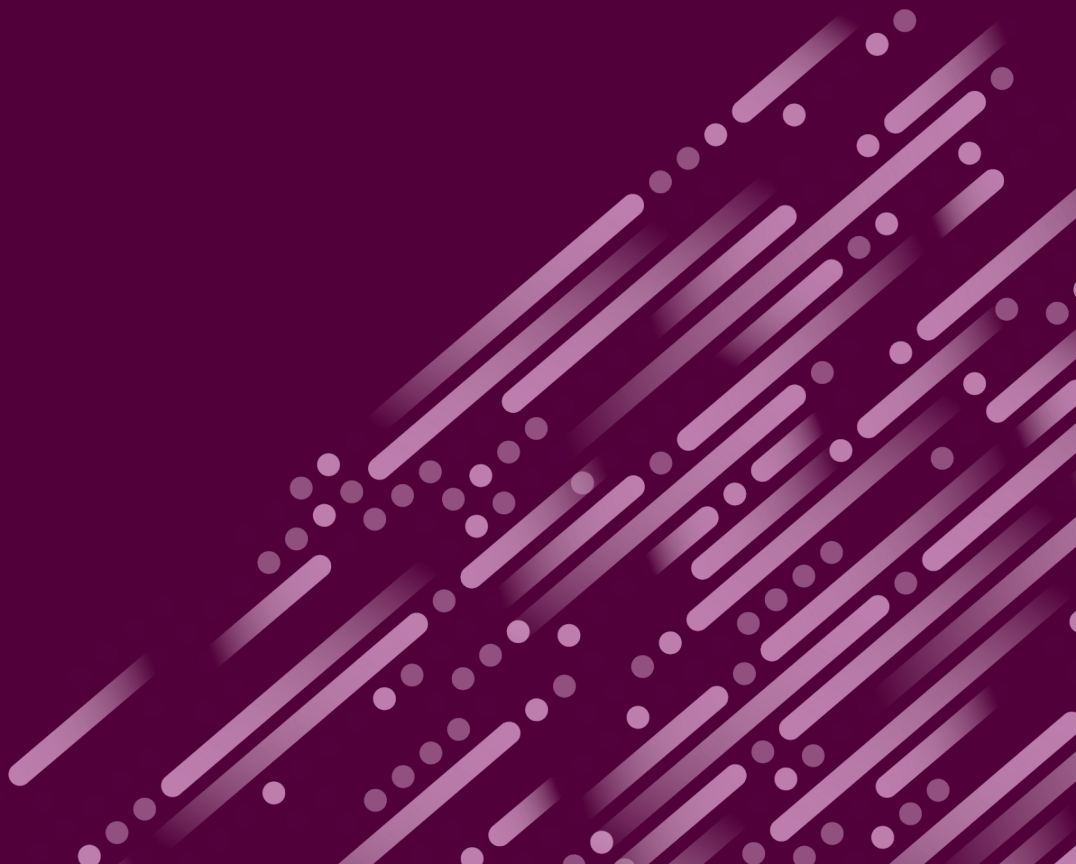
Pharma Intelligence
Informa

2021 ASCO Virtual Scientific Program Conference



2021 ASCO Virtual Conference

Day 2 Update - June 5th, 2021

The second day of the 2020 ASCO Virtual Scientific Program began with the Opening Session, which featured the President's Address. Key oral abstract sessions focused on pediatric oncology, metastatic breast cancer, and gastrointestinal cancer. Special case-based panel sessions focused on oligometastases in prostate cancer and the treatment of metastatic hepatocellular carcinoma.

Select highlights from our team of analysts are below:

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Overall survival (OS) with palbociclib + fulvestrant in women with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced breast cancer (ABC) (PALOMA-3), Abstract 1000

Updated overall survival (OS) results from a Phase III trial of postmenopausal patients (pts) with HR+/ HER2- advanced breast cancer (ABC) treated with fulvestrant ± ribociclib (MONALEESA-3), Abstract 1001

Updated OS results for CDK4/6 inhibitors Kisqali and Ibrance continue to show significant efficacy with no new safety signals in advanced HR+/HER2- breast cancer patients after prolonged follow-up. These updated results also provide additional efficacy information for specified subgroups, although supplementary studies are needed to confirm such benefits as these analyses are largely exploratory and have somewhat limited patient numbers.

In the Phase III MONALEESA-3 trial, after a median follow-up of 56.3 months, median OS for the Kisqali and fulvestrant combination was 53.7 months compared to 41.5 months in the placebo plus fulvestrant arm. The majority of the benefit was derived from first-line advanced patients: the median OS for the experimental arm was not reached and the median OS in the control arm was 51.8 months in this segment.

CDK4/6 inhibitors are known to be more effective in endocrine-sensitive populations and the combination achieved a statistically significant 7.2-month increase in median OS (49.0 months for Kisqali vs. 41.8 months for placebo; CI: 0.557-0.959) for endocrine sensitive patients. Endocrine-resistant patients experienced a numerically longer median OS, but this result did not achieve statistical significance (35.6 months for Kisqali vs. 31.7 months for placebo; CI: 0.451-1.473).

In the PALOMA-3 trial, median OS was 34.8 months for Ibrance plus fulvestrant compared to 28.0 months with placebo plus fulvestrant after a median follow-up of 73.3 months. The OS benefit was maintained in the subgroup of patients that have not received prior chemotherapy (39.3 months for Ibrance vs. 29.7 for placebo), but no OS benefit was seen in chemotherapy-experienced patients (24.6 months for Ibrance vs. 24.3 months for placebo). ESR1-mutants also experienced a significant improvement in OS with Ibrance treatment (27.7 months vs. 20.2 months). Patients with PIK3CA (27.7 months for Ibrance vs. 18.3 months for placebo; CI: 0.42-1.25) and TP53 mutations (23.0 months for Ibrance vs. 16.4 months for placebo; CI: 0.46-1.52) experienced numerical improvements in median OS.

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Phase III study of sacituzumab govitecan (Trodelvy) in relapsed/refractory triple-negative breast cancer (ASCENT), Abstract 1080

Gilead announced data from a subgroup analysis of the confirmatory Phase III ASCENT trial showing the utility of Trodelvy as a second-line treatment for patient with relapsed or refractory metastatic triple-negative breast cancer. The median overall survival (OS) in the subgroup of patients who recurred within 12 months after (neo)adjuvant therapy and had one line of prior therapy in the metastatic setting was an impressive 10.9 months in the Trodelvy arm, over double the 4.9 months median OS seen in the chemotherapy arm. Furthermore, Trodelvy demonstrated a notable 59% reduction in the risk of disease worsening or death over the chemotherapy arm (HR=0.41) and a meaningfully higher overall response rate (30% vs. 3%). The safety and tolerability results were in-line with previously reported data.

Similar to the results seen in the ITT population in ASCENT, the data from this subgroup analysis are remarkable in an area of high unmet medical need. Given that there are few alternative therapies available, these results support the use of Trodelvy as a new standard-of-care second-line therapy for this subgroup of patients.

Phase II study of second-/third-line venetoclax + fulvestrant versus fulvestrant alone in estrogen receptor (ER)-positive, HER2-negative, locally advanced, or metastatic breast cancer (VERONICA), Abstract 1004

Roche presented top-line results from the Phase II VERONICA study testing the combination of Venclexta and fulvestrant against fulvestrant monotherapy in patients with ER+, HER2- locally advanced or metastatic breast cancer who had received ≤2 prior lines of endocrine therapy and no prior chemotherapy in the advanced breast cancer setting and who had experienced disease recurrence or progression during or after CDK4/6 inhibitor therapy. Unfortunately, the doublet did not demonstrate a statistically significant difference in progression-free survival or clinical benefit rate over the fulvestrant monotherapy arm. Although the overall survival data was not mature at the primary analysis, the preliminary hazard ratio did not favor the combination regimen (stratified HR=2.56, p=0.0218). Furthermore, there was a higher rate of Grade 3–4 adverse events (AEs) observed in the Venclexta + fulvestrant arm as compared to the fulvestrant arm (26% vs. 11.8%). Biomarker analysis is on-going, but these results are quite disappointing and likely spell the end of development for this combination.

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Phase II study of regorafenib plus nivolumab in patients with mismatch repair-proficient (pMMR)/microsatellite stable (MSS) colorectal cancer (CRC), Abstract 3560

Abstract 3560 presented on the second day of ASCO 2021 was a readout of the top-line results from a single-arm, Phase II study of regorafenib plus nivolumab in patients with mismatch repair-proficient (pMMR)/microsatellite stable (MSS) colorectal cancer (CRC). The doublet appeared largely ineffective in the general patient population, with an ORR of 7.1% (all partial responses) observed, failing to replicate an earlier Phase Ib trial conducted in Japan. Interestingly, all of these responses occurred in patients without liver metastases, giving a higher ORR of 21.7% in this subgroup, suggesting to the experimenters that there may still be a justification to pursue further development of the combination. However, the regimen's safety profile was also discouraging, with a high rate of grade 3-5 treatment-related adverse events including one serious case of sepsis.

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Phase Ib/II open-label, randomized evaluation of atezolizumab (atezo) + Imprime PGG (Imprime) + bevacizumab (bev) vs regorafenib (rego) in microsatellite-stable (MSS) metastatic colorectal cancer (Morpheus-CRC), Abstract 3559

Roche presented results detailing the final analysis of Morpheus-CRC, a Phase Ib/II open-label, randomized evaluation of Tecentriq, Imprime PGG, and bevacizumab vs Stivarga in heavily pre-treated microsatellite-stable (MSS) metastatic colorectal cancer (mCRC). The triplet was well tolerated, with only 13% grade ≥ 3 treatment-related adverse events recorded (none of which were grade 5) compared to 62% for Stivarga. However, efficacy indices were consistently better in the Stivarga comparator arm.

Patients treated with the triplet showed a disease control rate of 13%, compared to 26% in those treated with Stivarga. Additionally, survival metrics were nearly halved in comparison to Stivarga; mPFS was 1.5 months vs. 2.8 months and mOS was 5.7 months vs. 10.2 months. No increased efficacy was found in any subsequent subgroup analyses and as such the experimenters were forced to concede that the trial had failed to reach its endpoints.

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Phase II study of idecabtagene vicleucel (ide-cel, bb2121), a BCMA-directed CAR T cell therapy, in relapsed and refractory multiple myeloma (KarMMa), Abstract 8016

Bristol Myers Squibb presented updated results for KarMMa, the pivotal Phase II study that supported approval of Abecma for fifth-line or later multiple myeloma (MM) in March 2021. With a median follow-up of 24.8 months in 128 patients treated with Abecma, the ORR was 73% and the rate of CR or stringent CR was 33%. The rate of very good partial response or better was 53%. Median duration of response was 10.9 months and increased with depth of response, with a median duration of response of 21.5 months for patients who achieved a CR or better. Median PFS was 8.6 months (95% CI: 5.6-11.6). The median OS was 24.8 months (95% CI: 19.9-31.2), and these survival data continue to mature.

In a small group of 15 patients who received three prior lines of therapy, the ≥CR rate improved to 53% but the median PFS was unchanged. OS was similar for patients < 65 (21.7 months) and ≥ 65 (28.3 months), for patients with or without extramedullary disease (lower range of 95% confidence interval of 21.3 months versus 20.2 months, respectively) and for patients who were or were not triple refractory (21.7 months versus 31.2 months). However, OS did decrease for patients with R-ISS stage III compared to R-ISS stage I-II (8.8 months versus 28.3 months, respectively).

Abecma continues to be investigated for earlier lines of therapy. KarMMa-3 is a randomized, controlled Phase III study versus SOC triplets for third-line or later MM. KarMMa-2 is a Phase II study evaluating Abecma in subjects with triple-class exposed fourth-line or later MM (Cohort 1), in subjects with early relapse after first-line treatment with or without autologous stem cell transplantation (ASCT) (Cohorts 2a and 2B, respectively), or in subjects with inadequate response post ASCT during initial treatment (Cohort 2c). Finally, KarMMa-4 is a Phase I trial evaluating Abecma in high-risk newly diagnosed MM.

Phase Ib/II trial of ciltacabtagene autoleucel, a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T-cell (CAR-T) therapy, in relapsed/refractory multiple myeloma (R/R MM) (CARTITUDE-1), Abstract 8005

Johnson & Johnson presented updated results for CARTITUDE-1, the pivotal Phase Ib/II trial supporting the biologics license application (BLA) for ciltacabtagene autoleucel (cilta-cel) currently under priority review with the FDA. CARTITUDE-1 enrolled fourth-line or later patients or patients who are double refractory to a proteasome inhibitor and an immunomodulator. With a median follow-up of 18 months for 97 patients, the ORR was 98%, with 80% of patients having a stringent CR (increasing from 67% presented at ASH 2020). Median PFS was 22.8 months while the 18-month OS rate was 81%.

Response rates were comparable across prespecified subgroups, including number of prior lines of treatment, extramedullary plasmacytomas and cytogenetic risk.

Although the efficacy seen with cilta-cel is remarkable, there are concerns over safety and tolerability. While the incidence of grade 3 or higher cytokine release syndrome (CRS) was greater for class competitor Abecma (4.1% versus 6.5%), the rate of serious neurotoxicity was higher for cilta-cel (10% vs 3%). Mitigation and management strategies are being implemented to identify and reduce the risk for neurologic adverse events (NEs). Such strategies include more effective bridging therapy to reduce tumor burden, early and aggressive treatment of CRS and NEs, and handwriting assessment and extended monitoring (Abstract 8028).

A confirmatory Phase III trial, CARTITUDE-4, is evaluating cilta-cel in MM patients who have previously received one to three lines of therapy. A Phase II study, CARTITUDE-2, includes separate cohorts for: (i) second to fourth line patients; (ii) patients with early relapse after front-line therapy; (iii) triple-refractory patients; (iv) front-line patients who had less than a CR following autologous stem cell transplant; and (v) newly diagnosed high-risk patients not eligible for transplant (cilta-cel will be administered after treatment with a Darzalex quadruplet).