KANTAR

WILL THESE 12 CANCER TRIALS CHANGE CLINICAL PRACTICE?

ASCO 2019 AND FUTURE DIRECTIONS IN ONCOLOGY

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Introduction

The American Society of Clinical Oncology's annual meeting in Chicago is the preeminent date on the cancer research calendar, and ASCO 2019 was no exception.

The healthcare professionals, pharmaceutical industry executives and global media that assembled at McCormick Place in June were presented with a wealth of new clinical data readouts from the oncology spectrum.

Kantar was on-site in Chicago gathering insights on the future direction for oncology. As the dust settles on ASCO 2019, and clinical practice begins to adapt to this year's meeting, this report picks out the key findings from 12 cancer trials, and we put the ASCO headlines into context for patients, prescribers and the pharmaceutical industry.

In doing so, our experts examine trial highlights from some of the biggest players in the business as well as those seeking to make a name for themselves. Looking at presentations by AstraZeneca, Gilead, Janssen, Merck & Co, Novartis, Seattle Genetics and others, we also dig into the robustness of the data and, for some medicines, find compelling levels of benefit.

The performance of emerging cancer medicines is put into context with currently available treatment options, and there is advice on what it means for the standard-of-care in oncology, as waves of exciting new approaches to treatment come into view.

From 'tumor agnostic' technology to a breakthrough in cancers involving KRAS mutations, antibody-drug conjugates to a maturing approach in immuno-oncology, there are many research advances in cancer to be excited about.

Bladder cancer – Enfortumab vedotin from Seattle Genetics and Astellas

Seattle Genetics has been making its name with antibody-drug conjugates, and its latest bladder cancer contender, enfortumab vedotin, was one of the drugs that impressed us at ASCO 2019, thanks to some strong data from a mid-stage trial.

Four checkpoint inhibitors – Roche's Tecentriq (atezolizumab), Merck & Co's Keytruda (pembrolizumab), AstraZeneca's Imfinzi (durvalumab) and Merck KGaA's Bavencio (avelumab) – are approved in bladder cancer, but have issues with low response rates.

Seattle Genetics and development partner Astellas are evaluating the drug in patients who have failed both platinum-based chemotherapy and checkpoint inhibitors. This is a cohort for whom prognosis is poor and few options are left other than another bout of chemotherapy.

THE PHASE 2 EV-201 TRIAL

Hoping to be able to offer a new option for these patients, the partners arrived at ASCO 2019 to present results from their Phase 2 EV-201 trial[1], which evaluated enfortumab vedotin in relapsed patients with locally advanced or metastatic bladder cancer. The data presented were from Cohort 1 of the trial, which evaluated enfortumab in relapsed patients who had been treated with a platinum and a checkpoint inhibitor.

In this study, the overall response rate in 125 treated patients was 44%, 12% had a complete response and 32% had a partial response. Adding to that it should be noted that responses to the treatment were similar across all the subgroups analyzed. The median duration of response was 7.6 months, the median progression-free survival (PFS) was 5.8 months and median overall survival (OS) was 11.7 months.

The toxicity profile was very favorable with the most common Grade 3 or greater adverse events being rash (12%), neutropenia (8%), anemia (7%), fatigue (6%), and hyperglycemia (6%). The discontinuation rate due to adverse events was 12%, of which peripheral neuropathy (50%, any grade) was the most common adverse event that led to discontinuation.

AN IMPORTANT ADVANCE IN BLADDER CANCER

Overall, the data look very promising and compares favorably, and in some cases exceeds that seen with checkpoint inhibitors used in the relapse setting. The EV-201 results on display at this year's ASCO meeting will most likely support accelerated approvals, and indeed various regulatory filings are planned for enfortumab later this year.

The FDA has already earmarked enfortumab vedotin as a breakthrough therapy, clearing the way for a potential fast six-month review. The U.S. regulator is keen to bring new cancer drugs to market and often grants 'accelerated approval', based on such data, with safety and efficacy confirmed by a larger final stage study.

For such an approval, we think the EV-201 data look to be sufficient. If seeking approval based on single-arm Phase 2 data, the primary endpoints to evaluate are ORR and that those responses are durable[2].

Although there's no definition for what constitutes 'durable' in this context, 7.6 months should definitely be in the required range. With no other approved or good alternative treatment options and good data, accelerated approval should be straightforward for Seattle Genetics and Astellas.

Serious side-effects, including one case of the skin disease Stevens-Johnson syndrome, as well as low rate of hyperglycemia and neuropathy in the Phase 2 trial, will be unlikely to deter the FDA from approval.

Such is their confidence in the EV-201 data that the companies filed the drug with the FDA shortly after ASCO and have already begun the Phase 3 EV-301 trial[3], comparing enfortumab vedotin versus physicians' choice of chemotherapy.

Breast cancer – Margetuximab from MacroGenics and Kisqali from Novartis

MacroGenics had already raised its profile in the oncology community ahead of ASCO 2019 with some surprise, early results for margetuximab, announcing that the Phase 3 SOPHIA trial met its primary endpoint of PFS[4]. Its presentation of results from the SOPHIA trial at ASCO was aimed at maintaining the drug's momentum and showing enough of a benefit in breast cancer.

Whether or not it could do that was a crucial question for MacroGenics, which is positioning margetuximab as a 'better Herceptin' with an improved antibody-dependent cell-mediated cytotoxicity (ADCC) and engineered to target specific genotypes that might be resistant to Herceptin (trastuzumab). In that context the company's choice to compare its candidate to Roche's blockbuster treatment certainly makes sense.

SOPHIA AND HER2 POSITIVE BREAST CANCER

The U.S. biotech tested margetuximab in combination with chemotherapy in HER2 positive breast cancer patients who had already failed to respond to several approved HER2-targeted therapies such as Herceptin.

In the SOPHIA trial[5], involving these very sick patients, the median PFS of patients treated with margetuximab and chemotherapy was 5.8 months compared to 4.9 months in patients treated with Herceptin and chemotherapy. The objective response rate, a secondary outcome measure in the SOPHIA study, was 22% in the margetuximab arm compared to 16% in the trastuzumab arm at data cut-off in October.

Among the 86% of patients carrying the CD16A genotype with a 158F allele, a pre-specified exploratory subpopulation in the study, PFS was prolonged by 1.8 months in the margetuximab arm compared to the trastuzumab arm (6.9 months versus 5.1 months).

The safety profile for the margetuximab arm was similar to that of the trastuzumab arm, with the exception of infusion-related reactions, which occurred at a higher frequency in the margetuximab arm (13% vs. 4%). However, these were mainly Grade 1-2 and manageable with pre-medication.

QUESTIONS ON CLINICAL-RELEVANCE

It is in patients with CD16A 158F allele where we would expect the drug to be most likely to be useful and ultimately succeed in the clinic. However, it remains to be seen whether the results for margetuximab will be viewed as clinically meaningful for all relapsed/refractory HER2+ metastatic breast cancer patients or only in a select population with specific CD16A polymorphisms. Certainly, demonstrating a significant OS improvement would go a long way towards this.

In patients with baseline measurable disease, margetuximab produced an overall response rate of 22% compared to 16% in the Herceptin arm. Immature OS analysis was shown, but there was not a significant difference. While the combination of margetuximab and chemotherapy did significantly improve PFS, the fact that it was only one month means that we still have questions about its clinical relevance for all patients.

There are also question marks about whether the small benefit compared with Herceptin will mean this drug is marketable in what is becoming an extremely competitive part of the market.

Herceptin's patent expired in the U.S. shortly after ASCO, opening the door to a gang of manufacturers with approved biosimilars that are as safe and effective as the original but considerably cheaper.

With these cut-price alternatives already on the market in the U.S. and Europe, it remains to be seen whether cash-strapped health systems will be prepared to pay for the marginal benefits seen so far from margetuximab.

KISQALI TARGETS EARLY STAGES OF BREAST CANCER

While MacroGenics is looking to take on Roche in the late stages of HER2-positive breast cancer, the other big Swiss pharma Novartis is targeting the early stages of the hormone receptor-positive (HR+) disease with Kisqali (ribociclib).

The cyclin-dependent kinase (CDK) 4/6 inhibitor is already approved in ER-positive, HER2-negative disease but facing intense competition from Pfizer's Ibrance (palbociclib) and Lilly's Verzenio (abemaciclib). However, Kisqali is approved as a first-line therapy in premenopausal patients for this indication, and results from MONALEESA-7 announced at ASCO 2019 will help encourage doctors to prescribe it.

A FIRST WITH MONALEESA-7

The MONALEESA-7 trial[6] is the first dedicated trial of endocrine therapy and a CDK4/6 inhibitor in premenopausal patients with hormone receptor (HR) positive advanced breast cancer. It not only demonstrated a doubling of median PFS with the addition of Kisqali, but also showed an OS improvement, making it the first trial of a CDK4/6 inhibitor in HR-positive breast cancer to show significant improvement in OS.

AN ADVANTAGE FOR NOVARTIS, BUT A GAME-CHANGER?

The MONALEESA-7 results will certainly give Novartis an edge in the peri-/premenopausal HR-positive breast cancer space. However, based on data from our CancerMPact Treatment Architecture[7], we see Pfizer's Ibrance as being fairly entrenched as standard of care in the post-menopausal space, and thus results from MONALEESA-7 may not be enough to change this.

Latest data from MONALEESA-7 announced at ASCO show OS was not reached in the treatment arm, where patients were treated with Kisqali plus endocrine therapy.

Patients in the control arm treated with endocrine therapy alone had a median overall survival of 40.9 months.

OS rates were, respectively, 71.9% vs. 64.9% at 36 months and 70.2% vs. 46.0% at 42 months.

Gastric cancer – Keytruda from Merck & Co

The KEYNOTE-062 study[8] was a trial with a lot going on across its three arms as Merck & Co sought to apply Keytruda (pembrolizumab) in first-line gastric cancer. It evaluated chemotherapy alone, which is the current standard of care in the indication, versus Keytruda as monotherapy, and versus Keytruda in combination with chemotherapy. What the trial wanted to determine was whether any of the two Keytruda arms had superior OS to chemotherapy alone.

Merck had a partial success. The company found the combination arm containing Keytruda and chemotherapy was not superior in OS to chemotherapy alone, but that the Keytruda monotherapy arm was non-inferior to chemotherapy alone.

In patients with a PD-L1 combined positive score (CPS) of one or more median OS was 10.6 months with Keytruda monotherapy, compared with 11.1 months for those treated with chemotherapy.

Results were better in patients with PD-L1 CPS of 10 or more – median OS in this group was 17.4 months in patients treated with Keytruda compared with 10.9 months in the control arm.

After 2 years, 39% of people taking pembrolizumab were alive compared with 22% of those taking chemotherapy.

ANOTHER TRIAL NEEDED?

Whether physicians will feel there's a compelling enough rationale to prescribe Keytruda in this setting will be determined by the market.

There are some groups that might stand to benefit a little bit from the monotherapy arm. Patients that are either too frail or too elderly to withstand the toxicity of chemotherapy might do better on Keytruda monotherapy, since it does have a much better adverse event profile relative to chemotherapy. Patients that have a really high expression of PDL-1 could also benefit, as this trial found that patients with a CPS score greater than or equal to 10 had seen an OS benefit of around 6.5 months relative to chemotherapy alone.

However, the study wasn't statistically powered for those sub-groups. So, if Merck wants to demonstrate Keytruda monotherapy was statistically meaningfully better than chemotherapy in OS it will likely need to run another trial.

That doesn't really bode very well for NCCN guidelines[9]. Currently, their recommendation in gastric cancer is category 2a evidence in the third-line but it's hard to imagine that the NCCN guidelines would be changed to recommend them as a first-line use.

Merck should also be a little concerned about its current third-line monotherapy label in gastric cancer. It's already pending confirmation by another trial, potentially this one but, given the strength of data that were presented at ASCO 2019, Merck will likely have to rely on another trial in order to maintain its current label with FDA.

Lymphoma – Yescarta from Kite Pharma

Gilead's Kite Pharma unit had a strong presence at ASCO, unveiling data about its already-approved CAR-T cell therapy, Yescarta (axicabtagene ciloleucel), from the company's ZUMA-1 study[10] in refractory diffuse large B-cell lymphoma. It's a study that has already been used to approve the therapy in this indication and now the company was looking to highlight its survival benefits.

YESCARTA IN THE ZUMA-1 STUDY

Kite offered an analysis in older patients of 65 years of age and above in the study, where there was a 92% overall response rate at a median 27.1 months, compared with 81% among patients under 65. After two years, 42% of those over 65 were still responding, compared with 38% in those under 65. In the older group 54% were still alive after two years compared with 49% in the under-65 group.

Moreover, complete response rates were 75% and 53% for the older and younger groups, respectively.

We also heard good news on the safety front, with new results presented showing that patients who had experienced a serious CAR-T side effect known as cytokine release syndrome (CRS) were able to be managed effectively with steroids, with no deaths due to adverse events.

The performance in the over-65s is important because patients with refractory large B-cell lymphoma who have exhausted treatment options and still face progressive disease are often older.

BUILDING MOMENT FOR ITS CAR-T FRANCHISE

Yescarta has been a slow-growing therapy for Kite and the company will be hoping the ZUMA-1 results will encourage greater use of the drug.

The new data could help Kite, and Gilead, consolidate its position in the market against Novartis' CD19 CAR-T Kymriah (tisagenlecleucel), which was the first CAR-T to market but has since fallen behind sales-wise thanks in part to manufacturing issues, despite what appears to be similar efficacy.

Lung cancer – BLU-667 from Blueprint Medicines

While the last few ASCO meetings have been dominated by the rise of checkpoint inhibition and CAR-T therapies, it seems that this year the long-awaited tumor-agnostic technology is beginning to gain traction.

One of the most notable examples of this was provided by Blueprint Medicines' BLU-667, which produced almost a 60% response rate in advanced lung cancer patients with RET mutations in the ARROW study[11]. It was only in a small study and results from a larger group are due at next year's ASCO. However, it stands out because BLU-667 is a drug with a new biomarker that may be used to better select patients.

ARROW HITS ITS TARGET

A RET inhibitor, BLU-667 was studied in patients with RET fusion-positive non-small cell lung cancer (NSCLC) in the registration-enabling ARROW study[12].

Overall response rate in the 57 response-evaluable patients was 56% and 91% of responding patients remained on the treatment. Blueprint's drug saw a 91% disease control rate and responses occur regardless of prior treatment or RET fusion genotypes.

Overall the company said BLU-667 demonstrated potent, durable and broad antitumor activity and was well tolerated, and it is in the process of expanding enrolment in the trial so that it can be used for regulatory submissions.

As far as the data presented at ASCO 2019 go, Blueprint cleverly targeted patients that usually don't have another alternative treatment beyond the current chemotherapy in use and, so far, BLU-667 has shown remarkable results for this population in the ARROW study.

Myeloma – Darzalex from Janssen and isatuximab from Sanofi

There were two standout drugs for myeloma on show at ASCO 2019. The first of these was Janssen's Darzalex (daratumumab) and its CASSIOPEIA study[13]. The CD38 inhibitor has already been shown to be an effective treatment option in multiple myeloma and is now looking to expand its list of approved indications to include the transplant eligible population.

To that end the Phase 3 CASSIOPEIA trial did not disappoint. This trial evaluating the combination of Darzalex plus VTD (Velcade, Thalidomide and Dexamethasone) met its primary endpoint of stringency response with an impressive hazard ratio. Clearly in Europe, where VTD is the standard of care, this combination is likely to be quickly adopted.

The primary endpoint of post-consolidation stringent complete response (sCR) was significantly better in a group of patients treated with Darzalex-VTd group (29%) versus 20% in a group treated with VTD.

However, in the United States, where Lenalidomide, Bortezomib, and Dexamethasone - or RVD - is the standard of care, physicians could be less likely to adopt this combination and instead may prefer to wait to see how the addition of Darzalex to RVD performs.

As well as Darzalex, ASCO 2019 saw another high-performing CD38 inhibitor, Sanofi's isatuximab, which was studied in relapsed/refractory multiple myeloma in the highly anticipated ICARIA Phase 3 trial[14]. This evaluated isatuximab to pomalidomide/dexamethasone and met its primary endpoint of PFS showing a 40% reduction in the risk of progression or death.

While data already suggest CD38-based regimens are very efficacious in the relapsed/refractory population, until there are studies on the sequencing of these two agents how physicians decide to use each inhibitor will come down to the details.

For example, a patient's co-morbidities such as COPD, a treatment's infusion time, and the choice of combination drug could all be ways physicians try to differentiate between these agents. To this point, also presented at ASCO 2019 were the results from the Phase 3 COLUMBA trial[15] which showed subQ Darzalex was non-inferior to IV Darzalex in relapsed refractory patients. The five-minute injection time compared to a seven-hour infusion time will make Darzalex an even more formidable competitor in this space and this study shows that subQ formulation is a viable option.

Our take-home message from these three studies is that they should further support the use of CD38 inhibitors in the multiple myeloma treatment landscape.

Pancreatic cancer – Lynparza from AstraZeneca and Merck & Co

Lynparza (olaparib) is already paving new ground in pancreatic cancer by aiming to establish a maintenance setting and patient segmentation based on a biomarker (gBRCA mt) in first-line metastatic disease.

At ASCO 2019 there were potentially practice-changing results for the AstraZeneca and Merck & Co drug from the Phase 3 POLO trial[16] that could provide hope for certain patients with pancreatic cancer.

While Lynparza looks like it will only work in a small percentage of patients, those whose disease has BRCA mutations, the data from the POLO trial suggest that this could be the first time a biomarker-selected targeted therapy has produced a survival benefit in a trial aimed at pancreatic cancer.

There is a pressing need for more treatments for pancreatic cancer, which is notoriously difficult to treat as symptoms usually only become apparent once the disease has spread through the body. Merck & Co's Keytruda (pembrolizumab) is a treatment option in another small patient group with 'MSI High' mutations, but that particular indication applies to all tumors, rather than just pancreatic cancer.

In their alliance AstraZeneca and Merck are developing Lynparza as a maintenance therapy, used to hold the disease in check after an initial round of platinum-based chemotherapy.

A TRUE 'WOW' MOMENT

The POLO data suggest that for between 4-7% of pancreatic cancer patients who have an inherited BRCA1 and/or BRCA2 mutation, Lynparza could stay progression, and possibly even cause tumors to shrink completely in a small number of cases.

Findings were based on 247 people screened for BRCA mutations from a sample of 3,315 people with pancreatic cancer. In the study, 92 people were randomly assigned to receive Lynparza, and 62 were assigned to placebo. Serious side effects (Grade 3 or greater adverse events) occurred in 40% of people taking Lynparza, compared with 23% in the placebo group, with 5.5% stopping Lynparza treatment compared with 1.7% on placebo.

The study showed that for pancreatic cancer patients with the germline BRCA gene, PFS was 7.4 months with Lynparza, compared with 3.8 months in those receiving placebo - a 47% reduction in risk of progression or death.

The median duration of response was 24.9 months, compared with 3.7 months on placebo, and after two years 22.1% of patients on Lynparza had no disease progression, compared with 9.6% for those treated with placebo.

Perhaps the biggest 'wow' moment from any of the presentations at ASCO 2019 was the POLO study's lack of OS data after two years. So many patients are still alive in the treatment arm that OS data are simply not yet available, a revelation that promoted some emotional responses from the study investigators.

BUT SOME PAUSE FOR THOUGHT

Due to the rare nature of the gBRCA mutations, and the need to maintain an initial response for at least 16 weeks, this trial was relatively small for a Phase 3, which may give clinicians some pause for thought when they consider the robustness of the data.

The lack of OS data could be an issue, with echoes here of Alimta (pemetrexed). Eli Lilly's drug was eventually approved as a maintenance therapy in NSCLC around a decade ago, despite similar issues with survival data. The likelihood is that final OS results will be equally influential for Lynparza in pancreatic cancer based on the POLO results.

Prostate cancer – Xtandi from Pfizer and Astellas and Erleada from Johnson & Johnson

Some of the biggest players in prostate cancer were also on hand at ASCO with new study results. Pfizer and Astellas highlighted the findings of the ENZAMET trial and Johnson & Johnson gave interim details of the TITAN trial, both in metastatic hormone-sensitive prostate cancer (mHSPC).

The ENZAMET trial[17] evaluated Xtandi (enzalutamide) in combination with standard of care therapy (LHRH analog with or without docetaxel) versus a nonsteroidal anti-androgen plus standard of care therapy in 1,125 patients with metastatic hormone-sensitive prostate cancer (mHSPC). Addition of Xtandi to standard of care demonstrated a three-year OS of 80% compared to NSAA plus standard of care at 72%, with a hazard ratio of 0.67.

Meanwhile, the TITAN trial compared Erleada (apalutamide) with placebo and androgen deprivation therapy (ADT) in patients with mHSPC. The results showed that adding Erleada to ADT improved radiographic PFS, with a reduction in risk of death or radiographic progression by 52%, and a 2-year OS of 82% compared to 74% for placebo plus ADT, a 33% reduction in risk of death.

Adverse events between the TITAN study's arms were similar, with a slight increase in rash with Erleada. Janssen has already filed for approval based on these results, and if it is licensed in this setting then we would expect the drug to help the company recover from the impending patent expiration for Zytiga (abiraterone acetate), which is also approved in mHSPC.

Both sets of trial results will support the use of Xtandi and Erleada in mHSPC patients, though a new filling for Xtandi may be held off until read out of OS results from ARCHES[18], an Astellas-sponsored Phase 3 trial of ADT with or without Xtandi in mHSPC.

TREATMENT SEQUENCING AND OTHER PROSTATE CANCER CHALLENGES

However, many questions remain. It's unclear how doctors will decide between Zytiga, Xtandi and Erleada, whether they can be used sequentially, and what the optimal sequence for doing so will be. Compounding that is the fact that existing data from metastatic castration-resistant prostate cancer, a more advanced form of the disease, show Xtandi is efficacious following Zytiga, but that the reverse is not true.

It's also important to note that as agents like Zytiga and Xtandi move into earlier treatment settings, that in turn leaves a void in the mCRPC setting, creating an unmet need for new agents.

As to whether Erleada will take the lead in mHSPC, the TITAN data certainly support the addition of Erleada to ADT for a broad range of patients in this setting. But looking ahead to the future shape of the prostate cancer landscape, it's clear the focus will be on increasing treatment intensity for mHSPC patients, overcoming the hurdle of differentiating between the agents and choosing the right therapy for the right patient.

Multiple indications – AMG-510 from Amgen

The annual ASCO meetings often see interesting stories emerge about Phase 1 data that generate hope for the future. One such story we saw at ASCO 2019 came from the data on Amgen's KRAS inhibitor AMG-510.

The drug is capturing the imagination of many oncologists at the conference as it works in a completely new way. Scientists have known about the role mutant KRAS cell switching proteins can play in cancers for decades, but have never been able to make a drug that interacts with the dysfunctional protein.

Researchers have previously unsuccessfully tried to develop inhibitors for KRAS due to the structure of the molecule, which has limited 'pockets' for a drug agent to bind to. However, one KRAS mutation, G12C, creates the target – the new cysteine residue – that allows binding of AMG-510 and irreversibly forces KRAS to an inactive state. The KRAS G12C mutation is found in around 13% of lung adenocarcinomas and 1-3% of other solid tumors and is implicated in cancers such as ductal carcinoma of the pancreas, and colorectal cancer.

A first-in-human Phase 1 trial[19] looked at AMG-510 in patients with KRAS G12C solid tumors, showing the drug to be very well tolerated, with none of the reported serious toxicities found to be drug related.

The activity was most promising in lung cancer. Out of 10 evaluable heavily pre-treated patients, only 1 patient had progressive disease – the rest had partial response (50%) or stable disease. In 18 patients with colorectal cancer, the best response was stable disease which was reported in two-thirds of patients. Although still promising, only time will tell whether the different results observed for colorectal cancer patients was due to different histologies, similar to the situation seen with BRAF inhibition.

These data were certainly very promising, but it should be emphasized that it was only a Phase 1 trial in a small number of patients. However, these data are promising enough to hope that physicians begin screening more of their patients with other indications to get them enrolled in a larger trial that should allow Amgen to have a relatively smooth path to approval.

Moreover, the strategy Amgen used to identify AMG-510 should give hope to other scientists looking for ways to inhibit previously undruggable targets. The next step for AMG-510 will be the results of a later Phase 2 study, which should be presented next year.

Even this early data from AMG-510 has been enough to drive up Amgen's share price considerably at a time when its blockbuster inflammatory diseases drug Enbrel could be set to lose its patent protection. We would expect more from AMG-510 in the future as further pharma companies look to exploit this potential new method of tackling cancer.

Conclusion

As the largest oncology meeting in the world, held at North America's biggest conference center, ASCO is always packed with new clinical trial readouts and thought-provoking study revelations. In 2019, the event saw checkpoint inhibition and CAR-T therapies consolidate their place in the treatment landscape, at the same time as long-awaited advances in tumor-agnostic technology began to emerge.

At the early stages of development, there was hope for the future from Amgen's Phase 1 trial of AMG-150, which works in a completely new way to target the KRAS G12C mutation. Seattle Genetics and Astellas' enfortumab vedotin also offered some strong mid-stage trial data for a cohort of patients for whom prognosis is poor and who have few options left.

From two of the biggest players in prostate cancer there were new study results that support the use of Pfizer and Astellas' Xtandi and Johnson & Johnson's Erleada in metastatic hormone-sensitive prostate cancer.

In breast cancer MacroGenics' quest to position margetuximab as a 'better Herceptin' through the SOPHIA trial advanced but posed more questions than could be answered by the data on show at ASCO 2019. Meanwhile, in the early stages of the disease Novartis' Kisqali demonstrated a doubling of median PFS with the addition of Kisqali, but also showed an OS improvement, making it the first trial of a CDK4/6 inhibitor in HR-positive breast cancer to show significant improvement in OS.

Merck & Co continued to try and expand Keytruda's position, with new data in gastric cancer, but whether physicians will feel there's a compelling enough rationale to prescribe Keytruda in this setting will be determined by the market. Furthermore, additional Keytruda trials will probably be needed to close the gaps left open by its latest readouts.

Gilead's Kite Pharma unit had a strong showing at ASCO and the new Yescarta data could help the company consolidate its position in the market against Novartis' CD19 CAR-T Kymriah, which was the first CAR-T to market but has since fallen behind sales-wise.

One of the most notable tumor-agnostic treatments on show at ASCO 2019 was Blueprint Medicines' BLU-667, which produced a 60% response rate in advanced lung cancer patients with RET mutations in the ARROW study. Although only a small study, it stands out because BLU-667 is a drug with a new biomarker that may be used to better select patients.

In myeloma the preeminent trials were the CASSIOPEIA study of Janssen's Darzalex and ICARIA study of Sanofi's isatuximab. While both drugs were efficacious in the relapsed refractory population, until there are studies showing the sequencing of these agents, or it's known whether having a CD38 backbone is beneficial, how physicians decide to use each inhibitor will come down to the details.

Lynparza is already paving new ground in pancreatic cancer and ASCO 2019 set up a real 'wow' moment for data from the POLO trial. The AstraZeneca and Merck & Co drug's study could be the first time a biomarker-selected targeted therapy has produced a survival benefit in a trial aimed at the notoriously difficult to treat pancreatic cancer. But it was the study's lack of OS data after two years. So many patients are still alive in the treatment arm that OS data are simply not yet available.

From these 12 cancer trials we can already see signs of practice-changing results for oncologists to digest and further work for pharmaceutical companies to identify how best to test candidates and prepare them for regulatory submissions.

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