IN THE NEWS

From ASCO 2022

During the first week of June 2022, a great deal of enthusiasm was noticeable at McCormick Place in Chicago, where around 31,000 oncology professionals attended the 2022 ASCO Annual Meeting in person for the first time since 2019. Importantly, a substantial number of attendees (a further 11,500, roughly) joined the meeting online, suggesting that contemporary scientific meetings should be held in hybrid formats to meet the needs of a diverse global community.

In line with ASCO Annual Meetings held in the past few years, equity was a central theme in the scientific programme. This focus was manifest in aspects ranging from the variety of topics covered in sessions to the choice of this year's recipients of Special Awards. In his opening address, Everett Vokes, this year's ASCO President, explained that the already existing disparities in cancer care have been exacerbated by the COVID-19 pandemic and various conflicts; and that ASCO is committed to closing this gap. The Opening Session also featured a sobering talk in which André Ilbawi provided details on the global extent of cancer care disparities, and called for the global oncology community to come together and for the main stakeholders to "invest in people".

As part of its commitment to improving equity, at this Annual Meeting ASCO and the Association of Community Cancer Centers presented a Joint Research Statement that provides recommendations to improve equity, diversity and inclusion in oncology clinical trials. Indeed, only 4–6% and 3–6% of trial participants in the USA describe themselves as Black or Hispanic, respectively, despite representing 15% and 13% of individuals with cancer in this country. The results of this and other initiatives to promote equity in clinical research are eagerly awaited, although improvements are likely to take a few years to materialize.

Finally, this Annual Meeting saw the presentation of results from a variety of potentially practice-changing clinical studies, which are discussed in several Research Highlights published in *Nature Reviews Clinical Oncology*. We look forward to learning about initiatives to improve equity and results from clinical research either in person or online at the 2023 ASCO Annual Meeting.

Diana Romero

GASTROINTESTINAL CANCER

Dostarlimab effective in dMMR LARC

Patients with mismatch repair-deficient (dMMR) metastatic colorectal cancers have superior responses to anti-PD-1 antibodies relative to their MMR-proficient counterparts. Nonetheless, many of these patients do not respond to therapy. Now, initial data from a single-arm phase II study involving patients with locally advanced rectal cancers (LARCs) reveal dramatically improved outcomes with the anti-PD-1 antibody dostarlimab in the neoadjuvant setting.

A total of 16 patients with dMMR stage II–III rectal cancer received neoadjuvant dostarlimab monotherapy for six months, followed by chemoradiotherapy and surgery. Patients with a complete response (CR) to neoadjuvant therapy received non-operative follow-up only. CR at 12 months or pathological CR (in patients undergoing surgery) were the primary end points.

At a median follow-up duration of 12 months, all patients included in the efficacy analysis had a clinical CR (objective response rate 100%). All evaluable patients remained disease-free at >12 months following completion of dostarlimab. All patients were able to avoid further treatment. Common grade 1–2 adverse events included rash or dermatitis (in 31% of patients), pruritus (25%), fatigue (25%) and nausea (19%). No grade ≥3 adverse events were observed.

Although preliminary, both in terms of number of patients included and follow-up duration, these findings demonstrate the potential for the 5–10% of patients with rectal cancers who have dMMR disease to receive curative therapy. These patients might also be spared chemoradiotherapy and/or surgery and the associated adverse events.

Longer-term follow-up data from this study are eagerly awaited, as are those from trials exploring the efficacy of neoadjuvant anti-PD-1 antibodies in other dMMR solid tumours. A deeper understanding of the mechanisms underlying these impressive clinical responses could facilitate improvements in the outcomes of patients with tumours of non-dMMR phenotypes.

Peter Sidaway

ORIGINAL ARTICLE Cercek, A. et al. PD-1 blockade in mismatch repair–deficient, locally advanced rectal cancer. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2201445 (2022)

HAEMATOLOGICAL CANCER

SHINE a light: frontline ibrutinib for MCL

Many patients with mantle cell lymphoma (MCL) are ineligible for intensive therapy, including allogeneic stem cell transplantation (ASCT), and are instead treated with bendamustine and rituximab (BR). Now, data from the phase III SHINE trial indicate that combining first-line BR with the BTK inhibitor ibrutinib, which has notable single-agent efficacy in later lines of treatment, substantially delays MCL progression.

SHINE involved 523 patients aged ≥65 with stage II–IV MCL for whom ASCT was not planned. The patients were randomly assigned (1:1) to receive six cycles of BR plus either continuous daily ibrutinib or placebo, as well as up to 12 additional maintenance doses of rituximab in those with an objective response. The primary end point was progression-free survival (PFS).

Despite broadly similar response rates, ibrutinib prolonged the median PFS duration by an impressive 2.3 years (80.6 months versus 52.9 months in the placebo group; HR 0.75; 95% CI 0.59–0.96; $P = 0.01$). By contrast, ibrutinib did not improve overall survival (55.0% versus 56.8% at 7 years; HR 1.07, 95% CI 0.81–1.40). However, fewer deaths were attributed to disease progression or treatment-emergent adverse events (TEAEs) in the ibrutinib group (22.2% versus 26.7%; HR 0.88, 95% CI 0.62–1.24). Moreover, only 19.9% of patients in the ibrutinib group received second-line therapy compared with 40.5% in the placebo group.

More patients in the ibrutinib group had grade 3–4 TEAEs (81.5% versus 77.3%), with notably higher rates of pneumonia, lymphopenia, anaemia, rash, diarrhoea, hypertension and atrial fibrillation, as well as TEAEs leading to death (10.7% versus 6.1%). Nevertheless, the time to worsening of patient-reported symptoms or disease-related concerns was similar in both groups (HR 1.02, 95% CI 0.83–1.26).

These results demonstrate the efficacy of combining ibrutinib with BR in patients with MCL. However, the optimal sequencing of these therapies, as well as other approved treatments, remains unclear.

David Killock

ORIGINAL ARTICLE Wang, M. L. et al. Ibrutinib plus bendamustine and rituximab in untreated mantle-cell lymphoma. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2201817 (2022)