BSBMTCT position statement on the use of ruxolitinib in GvHD

27th September 2022

Statement:

The BSBMTCT, on behalf of its members, strongly recommends that **ruxolitinib should be made available equitably across the United Kingdom** for patients with grade II-IV steroid refractory acute Graft versus Host Disease (GvHD) or chronic GVHD refractory to high-dose systemic corticosteroid therapy, either with or without concurrent calcineurin inhibitor (tacrolimus/ciclosporin), sirolimus or mycophenolate mofetil.

Background:

Ruxolitinib (brand name Jakafi) is a selective oral JAK1 and JAK2 inhibitor, which is currently approved by the FDA, EMA and MHRA for treatment of acute and chronic GvHD. In GvHD, this novel agent works by inhibiting T-cell proliferation and reduction in cytokines such as IL-1, IL-6, IL-12, IL-17, TNF-α, and IFN-γ. Despite its immunomodulatory effect, it has no impact on graft versus leukaemia effect, an excellent safety profile and it is simple to administer.

Early evidence of its efficacy was reported in retrospective analysis [1] involving 54 patients with steroid refractory acute GvHD showing an overall response rate (ORR) of 81.5% in patients treated with ruxolitinib. A prospective single arm multicentre, open label, phase 2 study (REACH-1; NCT02953678) confirmed an ORR at day 28 of 54.9%. Best ORR at any time was 73.2%. The US Food and Drug Administration (FDA) approved the use of ruxolitinib for the treatment of glucocorticoid-refractory acute GvHD in patients 12 years of age or older in May 2019 based on outcomes in this cohort of patients [2]. This study was followed by a multicenter, randomized, open-label, phase 3 trial (REACH 2) comparing the efficacy of ruxolitinib in acute GvHD compared to investigator's choice of therapy. This study [3] involved 309 patients and showed an ORR at day 28 to be significantly superior in the ruxolitinib arm compared to the control group (62% vs. 39%).

In September 2021, the FDA approved ruxolitinib for chronic GvHD after failure of one or two lines of systemic therapy in adult and paediatric patients older than 12 years. This decision was based on outcome of a randomized, open-label, multicenter clinical trial of ruxolitinib compared to best available therapy (BAT) for corticosteroid-refractory chronic GvHD (REACH-3, NCT03112603). The trial randomized 329 patients to receive either ruxoltinib or BAT and confirmed ruxolitinib to be superior to BAT. The major efficacy outcome used to support approval was ORR based on 2014 NIH Response Criteria (Overall response at week 24 was 49.7% with ruxolitinib compared to 25.6% for the control group). A best overall response up to week 24 was observed in 76.4% of patients in the ruxolitinib group and in 60.4% in the control group [4].

Several other studies have confirmed the efficacy of ruxolitinib describing real world data [5,6,7,8,9]. Ruxolitinib has also been recommended as a treatment option for acute and chronic GvHD within recent EBMT consensus guidelines [10].

Full prescribing information is available in following link:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202192s023lbl.pdf

Ruxolitinib access in England:

In 2020, NHS England approved the use of ruxolitinib in grade II-IV steroid refractory acute GvHD or chronic GvHD refractory to high-dose systemic corticosteroid therapy either with or without concurrent calcineurin inhibitor (CNI) (tacrolimus/ciclosporin), sirolimus or mycophenolate mofetil (MMF) as a part of a COVID-19 rapid policy [11]. This not only provided patient access to a highly effective treatment for GvHD but also helped reduce hospital attendance when compared to alternative options such as extracorporeal photopheresis (ECP). Following termination of COVID-19 related policies, this approval was withdrawn on the 31 March 2022 and Blueteq forms for these policies were disabled. Providers are allowed to continue this therapy in the patients who had initiated treatment under the previous policy but no new patients can be commenced on ruxolitinib. In Wales and Scotland, access to ruxolitinib for GvHD continues to be available via local commissioning policies.

The National Institute of Health and Care Excellence (NICE) has identified ruxolitinib as suitable for NICE appraisal for both the chronic and acute GvHD indications. However, the pharmaceutical company manufacturing ruxolitinib, Novartis, has informed NICE that it will not provide evidence for the appraisal of ruxolitinib for treating chronic or acute graft versus host disease at this time and hence NICE is no longer considering its approval. NHS England has also refused to reinstate the rapid commissioning policy. At present, ruxolitinib approval is dependent on either individual funding request or local approval by individual trusts which does not guarantee an equitable access to this drug for patients in the UK.

The BSBMTCT, on behalf of its members, strongly feels that this highly effective treatment should be made available for patients equitably across the United Kingdom.

References:

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