Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter

Evidence is Lacking for the NHS England Interim Guidance for Managing Metastatic Non-small Cell Lung Cancer in the COVID-19 Pandemic

Madam — Immunotherapy has improved non-small cell lung cancer (NSCLC) survival [1]. The COVID-19 pandemic has led NHS England to suggest stopping maintenance pemetrexed and using pembrolizumab monotherapy in patients with a tumour proportion score (TPS) < 50% [2].

Before immunotherapy, pemetrexed improved median overall survival (mOS) by 2.9 months [3,4]. In KEYNOTE-189, adding pembrolizumab improved mOS across all TPS subgroups [5]. However, the mOS in the TPS <1% subgroup (17.2 months) was similar to pemetrexed maintenance studies. Given the higher rate of severe adverse events (71.9% versus 66.8%) and immune-related adverse events (10.9% versus 4.5%) with immunotherapy [5], pemetrexed monotherapy may be preferable in TPS < 1% patients.

KEYNOTE-042 randomised untreated metastatic NSCLC patients to pembrolizumab monotherapy or chemotherapy, showing a mOS of 20, 17.7 and 16.7 months in TPS groups >50%, >20%, >1%, respectively [6]. This was inferior to the mOS observed in KEYNOTE-189 (TPS 1–49%: 21.8 months; TPS < 1%: 17.2 months) [5]. KEYNOTE-407 assessed triple therapy in metastatic squamous NSCLC and showed a superior progression-free survival of 7.2 months (TPS 1–49% group) and 6.3 months (TPS < 1% group) [7] compared with the progression-free survival of 6.2 months (TPS > 20% group) and 5.4 months (TPS > 1% group) in KEYNOTE-042 [6]. Critically, in KEYNOTE-042, up to 72% of the lower TPS subgroups included patients with a TPS >50%, probably inflating the mOS observed [6].

The survival advantages of triple therapy come at a cost of higher rates of adverse events (71.9% versus 18%), particularly myelosuppression (15% versus <2%) [5,6]. Immune-related adverse events can be equally challenging to manage and may present with features that overlap with COVID-19 infection. Using immunosuppression was initially thought to be detrimental with COVID-19 [8], but the awaited RECOVERY trial publication may clarify this issue [9].

There is limited evidence for the efficacy of pembrolizumab monotherapy in TPS 0–49%. The European Medicines Agency has declined licensing for this indication [10]. Despite interim guidance, there is an efficacy and safety trade-off that must be acknowledged.

Conflicts of interest

The authors declare no conflicts of interest.

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