Real-world experience of the tolerability of neo-adjuvant chemotherapy and immunotherapy in the treatment of early triple negative breast cancer

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Introduction

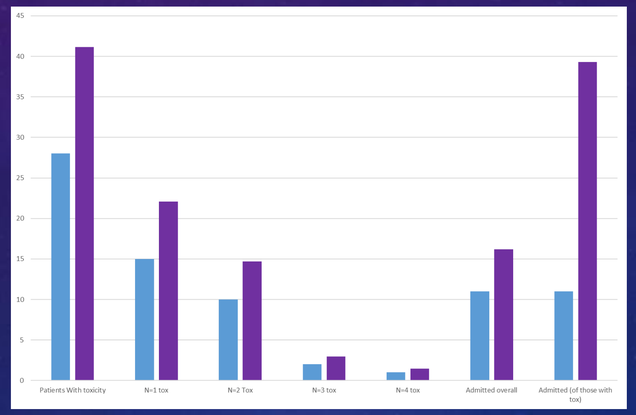
The KEYNOTE-522 clinical trial illustrated that the addition of pembrolizumab to neoadjuvant chemotherapy was clinically beneficial with statistically significant complete pathological response rates and, latterly, overall survival benefit[1,2]. Within the trial, adverse events of interest/ immune related adverse events (irAEs) occurred in 38.9% of patients and grade 3 or higher toxicities occurred in 12.9% of patients with 3.8% of patients experiencing severe skin reactions and 1.3% experiencing adrenal insufficiency[1].

Methods

Patients received treatment as standard of care at the Clatterbridge Cancer Centre, a tertiary cancer centre with a population of 2.4mn. A retrospective review of the patients receiving neoadjuvant chemotherapy and immunotherapy in combination were reviewed to assess the tolerability of treatment in the neoadjuvant phase. For toxicities commonly associated with chemotherapy such as diarrhoea and hepatitis were only considered to be an irAEs following clinical review.

Results

Since December 2022 there have been 68 patients commenced on treatment. Of them 41.2% (n=28) have experienced irAEs. Of these 28 patients, 53.5% (n=15) have experienced one organ/system toxicity and 46.4% (n=13) have experienced irAEs affecting more than one organ/system, with one patient experiencing 4 separate irAEs. Of the 45 irAE episodes 80% (n=36) ≥ grade 2 with 36% (n=16) ≥ grade 3. In addition to this 39% (n=11) of patients with irAE required admission for treatment, 16% of the overall treated population. Clinically significant irAEs included hepatitis (14%; 10/68); endocrinopathies (11.8%; 8/68); skin toxicity (10.2%; 7/68); colitis (8.8%; 6/68) and pneumonitis (7.3%; 5/68).



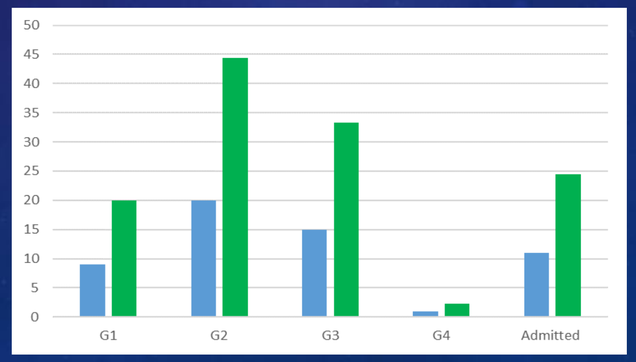


Figure 1: 1A Incidence of multiple toxicities experienced by patients (light blue=N; purple=%, total N=68 patients)
1B Severity of toxicity experienced by [patients (light blue=N; green = %. Total toxicities overall N=45)

Conclusions

In this early cohort of patients treated with Neoadjuvant chemotherapy and immunotherapy in combination the frequency of adverse events was notably higher than in the landmark trial. There were an high incidence of skin toxicity and endocrinopathies in line with the trial findings however other organ systems were affected including the liver, lungs and GI tract. Whilst further real world data is needed, this data suggests that comprehensive counselling, recognition and management of patients treated neoadjuvantly is required to ensure the increased oncological benefit of the regime can be realised and definitive treatment delivered.

References

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2. Merck Announces Phase 3 KEYNOTE-522 Trial Met its Overall Survival (OS) Endpoint in Patients With High-Risk Early-Stage Triple Negative Breast Cancer (TNBC) - Merck.com

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