TOXICITY PROFILES OF WEIGHT-BASED 2-WEEKLY AND FLAT-DOSE 4-WEEKLY NIVOLUMAB REGIMEN – A REAL-WORLD AUSTRALIAN CENTRE EXPERIENCE

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Background Anti-PD1 inhibitor nivolumab gained US FDA approval in 2014 using a weight-based, 2-weekly regimen (Q2W). In 2018, US FDA approved a flat-dose, 480mg 4-weekly regimen (Q4W) based on quantitative pharmacokinetic modelling.1,2 Whilst the Q4W regimen has since been widely adopted, real-world data on safety across various tumour types remain lacking, with anecdotal reports of differing toxicity profiles due to increased drug exposure.

Methods We conducted a single-centre, retrospective analysis on adults receiving nivolumab for any tumour or treatment intent in Calvary Mater Newcastle between Jan 2015 and July 2020, collecting information on treatment and immune-related serious adverse events (SAEs). Those receiving concurrent systemic therapy other than nivolumab were excluded. Toxicity profiles, including incidence rate, types of events, and timing of onset, were compared, as were SAEs’ impact on nivolumab treatment intention long term.

Results 137/43/35 patients received nivolumab on Q2W/Q4W/Q2W switch to Q4W (Q2-4W) regimen. Baseline characteristics were unequal, particularly the dominant tumour types (78% NSCLC in Q2W, 74% melanoma in Q4W) and treatment intention (palliative intent 96% in Q2W vs. 37% in Q4W). Q4W cohort received 29% higher nivolumab dose per week of treatment than Q2W. 23 (17%) and 7 (16%) patients experienced 24 and 9 SAEs on Q2W/Q4W, respectively. SAE per 100 person-weeks on nivolumab was higher in Q4W than in Q2W (0.99 vs. 0.64, OR 1.55), but the difference was statistically insignificant (95% CI 0.63-3.44, p=0.26, table 1). Q4W was associated with significantly earlier SAE onset than Q2W (4.1 vs. 17.7 weeks, OR 4.32, p=0.012, figure 1). Q4W was associated with more colitis (44 vs. 21%) with earlier onset (4.1 vs. 11 weeks). SAEs caused more nivolumab discontinuation in the Q2W cohort, but the difference was statistically insignificant (83% vs. 43%, OR 1.93, p=0.29). Choice of nivolumab regimen did not influence the rate of SAEs in those receiving radiotherapy. Most SAEs required systemic corticosteroid therapy (20/23 vs. 6/7) and hospitalisation (18/23 vs. 7/7), but the majority resolved within six months at a similar rate (71% vs. 75%). The SAE rate was low in the Q2-4W (6%), with no treatment discontinuation.

Conclusions Q4W nivolumab regimen was not associated with an increased incidence of SAE compared to Q2W but was associated with earlier onset with a penchant for colitis. Further research may identify unique toxicity signatures associated with different scheduling and help individualise patient treatment.

REFERENCES

Ethics Approval Hunter New England Human Research Ethics Committee provided consent to collect and analyse data as the study involved pre-existing, non-identifiable data (authorisation 2020/STE03882)