Daratumumab/obinutuzumab

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Various toxicities: 14 case reports

In a monocentric retrospective study, 14 patients (13 males and 1 female) aged 6.0–18.8 years were described, who developed hypogammaglobulinaemia, neutropenia or infusion-related-reaction manifested as vomiting, urticaria, mild transient bronchospasm, throat itching and labial oedema during off label treatment with obinutuzumab or daratumumab for steroid-dependent nephrotic syndrome (SDNS) [*duration of treatments to reactions onsets not stated*].

The patients with SDNS were initially treated with B cell depleting agents (rituximab or ofatumumab). However, nephrotic syndrome relapsed. The patient had previously received various immunosuppressive medications. Afterwards, they received off label treatment with single IV dose of obinutuzumab 230–1000 mg/1.73m^2 infusion over 4h, injected at day 0. At day 14, the patients received off label treatment with daratumumab 445–1000 mg/1.73m^2 injection, infused over 4h. Prior to each infusion, patients received systematic premedication with paracetamol [acetaminophen] methylprednisolone, and dexchlorpheniramine. Concomitantly, they also received oral immunosuppressants. During off label treatment, all the 14 patients developed hypogammaglobulinaemia with plasma immunoglobulin G (IgG) levels 2–6 g/L, secondary to obinutuzumab and daratumumab. Of the 14 patients, four patients showed a significant decrease in plasma IgG levels, while one had undetectable plasma immunoglobulin A (IgA).

Around 13 patients with hypogammaglobulinaemia were treated with IV immune-globulin. Around 18 months following obinutuzumab and daratumumab therapy, one patient developed COVID-19 with isolated fever secondary to hypogammaglobulinaemia, during 36h and completely recovered without any respiratory signs. Mild infusion-related reactions were reported in three patients during obinutuzumab infusion manifested as vomiting (Patient 4 and Patient 10) and urticaria (Patient 3). Similarly, four patients developed infusion-related reactions during daratumumab infusion manifested as mild transient bronchospasm, throat itching and labial oedema (Patient 2, 12, 13 and 14). Mild transient neutropenia (below 1500 /mm^3, observed by months 1, 4, and 12) was reported two patients (Patient 3 and Patient 9), which was attributed to obinutuzumab and daratumumab. The neutropenia did not require any specific treatment [*not all outcomes stated*].

Dossier C, et al. A global antiB cell strategy combining obinutuzumab and daratumumab in severe pediatric nephrotic syndrome. Pediatric Nephrology 36: 1175-1182, No. 5, May 2021. Available from: URL: http://doi.org/10.1007/s00467-020-04811-0

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