PROPOSAL TO REDUCE OBSERVATION TIME POST FIRST SUBCUTANEOUS INJECTION OF DARATUMUMAB

Situation:

Patients scheduled to commence SACT regimens containing subcutaneous daratumumab (DARZALEX brand) at BHOC are usually being observed on the day unit for 6 hours following the first injection to monitor for signs of hypersensitivity reactions or anaphylaxis.
However, the use of different protocols suggesting shorter monitoring times has caused inconsistencies in practice in the past, resulting in a few patients being monitored for less time when the same drug was being used.
This has highlighted the need for a standardised plan as well as an interest to analyse the incidence of adverse reactions in our local setting.
The audit question is whether a reduction of observation time to 4 hours after the first injection is reasonable and safe, the main audit objectives being to potentially improve patient experience as well as to optimise the patient flow on the day unit.

Background:

SPC guidance suggests that DARZALEX 1800 mg can cause severe and/or serious infusion-related reactions (IRRs), including anaphylaxis. In clinical studies, approximately 9% (74/832) of patients experienced an IRR. Most IRRs occurred following the first injection and were grade 1-2. IRRs occurring with subsequent injections were seen in 1% of patients. The median time to onset of IRRs following DARZALEX injection was 3.2 hours (range 0.15-83 hours). Most IRRs occurred on the day of treatment. Delayed IRRs have occurred in 1% of patients.
The European Medicines Agency mentions that in clinical studies (monotherapy and combination treatments; N=832) with DARZALEX subcutaneous formulation, the incidence of any grade IRRs was 8.2% with the first injection of DARZALEX (1800 mg, week 1), 0.4% with the week 2 injection, and 1.1% with subsequent injections. Grade 3 IRRs were seen in 0.8% of patients. No patients had grade 4 IRRs.
However, both guides do not specify a recommended observation period for the first injection, therefore BHOC staff usually rely on protocols released by SWAG where an observation period of 6 hours post first injection is advised. If patients experience no IRR, there is no observation period recommended for subsequent doses.
Other protocols advise shorter monitoring period like Thames Valley and University Hospital Southampton: in both cases they recommend 4 hours observations following the first injection of DARZALEX.

Assessment:

Data has been pulled retrospectively from alerts on ChemoCare, together with nursing and medical documentation on CareFlow and Evolve. Consequently, the collected information has been analysed.

Of a total of 70 patients that were scheduled to commence subcutaneous daratumumab within the Trust between May 2020 and December 2023:

- 3 patients did not commence it as they either declined treatment or were too unwell in ITU.
- 5 patients had missing notes from CareFlow or Evolve (they underwent treatment in Weston General Hospital or as inpatients).

Out of the 62 patients remaining, 5 patients (8.06%) experienced an IRR that could be split as follows:

- 1 patient (1.61%) within 1 hour of injection (feeling generally unwell, clammy and abdominal cramping).
- 2 patients (3.23%) within 3 hours of injection (one developed shaking and rigors, other one headaches, palpitations and rhinitis).
- 2 patients (3.23%) between 4 and 6 hours of injection but both had been discharged from BHOC. The first one was discharged earlier with safety netting most likely due to monitoring time finishing past day unit closing time: 5.5 hours post injection he developed a rash covering > 30% of body surface area and temperature rise to 37.9°C, they were then reviewed in SDEC and discharged with topical steroids and oral antihistamines. The second one rang their specialist nurse the day after the injection, stating they experienced rigors back home 6 hours after the injection, symptom which subsided after 2 hours without intervention. Unclear documentation as to why they had been discharged earlier.

Recommendations:

Based on the gathered data, considering the low percentage of patients who developed an IRR between 4 and 6 hours, we would like the SACT group to formally take into consideration the change in BHOC local practice to: 4 hours monitoring time post first injection of subcutaneous daratumumab. This change would be accompanied by thorough patient education from the nursing staff, as well as close safety netting regarding signs and symptoms to look out for at home and how to report promptly any adverse reactions to the 24-hour helpline.