Tocilizumab (for cytokine release syndrome)

Indication
Tebentafusp-induced cytokine release syndrome (CRS)

Regimen details
Tocilizumab 8mg/kg in 100ml 0.9% sodium chloride over 1 hour

Cycle frequency
See below

Number of cycles
If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered. The interval between consecutive doses should be at least 8 hours

Administration
Tocilizumab should be added slowly to a 100ml bag of 0.9% sodium chloride, after removing an equivalent volume (so the total volume = 100ml). Mix the solution by gently inverting the bag. Do not shake the bag.
Tocilizumab should be infused over 1 hour

Pulse, blood pressure, temperature & respiration rate for any signs of hypersensitivity reaction. Observations should be measured after 15 minutes, then every 30 minutes until 1 hour post infusion

In the event of a hypersensitivity reaction or anaphylaxis, stop the infusion and administer appropriate supportive care

Dose banding:

Weight	Dose	Volume of tocilizumab 20mg/ml concentrate to be added	Vials to be supplied
< 41kg	8mg/kg, rounded to nearest 20mg	Variable	Variable
≥ 41kg and ≤ 45kg	360mg	18ml	1 x 200mg & 2 x 80mg
≥ 46kg and ≤ 55kg	400mg	20ml	1 x 400mg
≥ 56kg and ≤ 65kg	480mg	24ml	1 x 400mg & 1 x 80mg
≥ 66kg and ≤ 80kg	600mg	30ml	1 x 400mg & 1 x 200mg
≥ 81kg and ≤ 90 kg	680mg	34ml	1 x 400mg, 1 x 200mg, 1 x 80mg
≥91kg	800mg	40ml	2 x 400mg

Pre-medication
None required

Emetogenicity
Minimal

Additional supportive medication
None required

Extravasation

Neutral

Investigations

Patients are being closely monitored following administration of tebentafusp, refer to tebentafusp protocol for monitoring guidance

Dose modifications

Do not adjust the dose of tocilizumab

Adverse effects –

for full details consult product literature/ reference texts

Infections
Viral reactivation
Hypersensitivity reactions
Hepatotoxicity
Neutropenia
Thrombocytopenia
Hyperlipidaemia

Significant drug interactions

– for full details consult product literature/ reference texts

Interaction studies have only been performed in adults.
Concomitant administration of a single dose of 10 mg/kg tocilizumab with 10-25 mg MTX once weekly had no clinically significant effect on MTX exposure.
Population pharmacokinetic analyses did not detect any effect of MTX, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids on tocilizumab clearance.
The expression of hepatic CYP450 enzymes is suppressed by cytokines, such as IL-6, that stimulate chronic inflammation. Thus, CYP450 expression may be reversed when potent cytokine inhibitory therapy, such as tocilizumab, is introduced.
In vitro studies with cultured human hepatocytes demonstrated that IL-6 caused a reduction in CYP1A2, CYP2C9, CYP2C19 and CYP3A4 enzyme expression. Tocilizumab normalises expression of these enzymes.
In a study in RA patients, levels of simvastatin (CYP3A4) were decreased by 57% one week following a single dose of tocilizumab, to the level similar to, or slightly higher than, those observed in healthy subjects.
When starting or stopping therapy with tocilizumab, patients taking medicinal products which are individually adjusted and are metabolised via CYP450 3A4, 1A2 or 2C9 (e.g. . methylprednisolone, dexamethasone, (with the possibility for oral glucocorticoid withdrawal syndrome), atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin, or benzodiazepines) should be monitored as doses may need to be increased to maintain therapeutic effect. Given its long elimination half-life (t1/2), the effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy.

Additional comments

References

RoActemra SPC - https://www.medicines.org.uk/emc/product/6673/smpc

LTH guideline for the use of tocilizumab in patients with suspected SARS-CoV-2 - http://lthtr-documents/current/P1892.pdf

THIS PROTOCOL HAS BEEN DIRECTED BY DR BOARD, DESIGNATED LEAD CLINICIAN FOR MELANOMA

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: November 2021
Review: November 2023
VERSION: 1