Indication	As part of DA chemotherapy for previously untreated CD33 positive acute myeloid leukaemia (not APL)
Treatment Intent	Curative
Frequency and number of cycles	2 cycles of induction chemotherapy followed, for patients experiencing a complete remission following induction, by up to 2 consolidation courses (gemtuzumab given with cycle 1 of Induction and up to 2 cycles of consolidation)
Monitoring Parameters pre-treatment	• ECG before first cycle • LFTs, FBC and U&Es before start of treatment, prior to each DOSE of gemtuzumab ozogamicin and before induction cycle 2 or more frequently as clinically indicated. Proceed with first course of treatment regardless of FBC. Proceed with Cycle 2 at haematological recovery. Proceed with consolidation treatment when neutrophils > 1.0 x 10^9/L and platelets >100 x 10^9/L • In patients with hyperleukocytic (leukocyte count ≥ 30x10^9/L) AML, cytoreduction is recommended either with leukapheresis, oral hydroxyurea or AraC with or without hydroxyurea to reduce the peripheral white blood cell (WBC) count 48 hours prior to administration of gemtuzumab ozogamicin. • Withhold anti-hypertensive medications 12 hours before and 12 hours after treatment. • **Renal impairment:** No dose adjustment of gemtuzumab ozogamicin is required in patients with mild to moderate renal impairment. No data in severe renal impairment although gemtuzumab does not undergo renal clearance. Daunorubicin: Serum Cr 105 – 265 µmol/L give 75% dose; SrCr > 265 µmol/L give 50% dose. Cytarabine (doses at 1000mg/m^2): CrCl >60ml/min give 100% dose; CrCl 46-60ml/min give 60% dose; CrCl 30-45ml/min give 50% dose; CrCl <30ml/min contra-indicated. • **Hepatic Impairment**: No dose adjustment of gemtuzumab ozogamicin is required in patients with total bilirubin ≤ 2 × ULN and aspartate AST/ ALT ≤ 2.5 × ULN. Treatment must be withheld until these parameters are met before further doses. Daunorubicin: bilirubin 20 – 50 µmol/L give 75% dose; bilirubin > 50 µmol/L give 50% dose. Cytarabine: bilirubin > 34 µmol/L d/w consultant who may consider giving 50% dose. Escalate dose in subsequent cycles in the absence of toxicity. • **Hepatotoxicity:** Including hepatic venoocclusive disease/sinusoidal obstruction syndrome (VOD/SOS), (Common symptoms to include hepatomegaly, right upper quadrant pain, jaundice, and ascites). Dose interruption or discontinuation may be required if hepatic toxicity occurs. In the event of VOD/SOS gemtuzumab should be discontinued. • **Tumour Lysis Syndrome: (TLS)** Monitor for signs and symptoms of TLS. Appropriate measures (hydration, allopurinol, rasburicase) must be taken to prevent hyperuricemia as clinically indicated.

	• **Infusion related reactions:** Infusion should be interrupted immediately for patients who develop evidence of severe reactions, especially dyspnoea, bronchospasm, or clinically significant hypotension. Patients should be monitored until signs and symptoms completely resolve. Discontinuation of treatment should be strongly considered for patients who develop signs or symptoms of anaphylaxis, including severe respiratory symptoms or clinically significant hypotension. Gemtuzumab ozogamicin should be administered under close clinical monitoring, including pulse, blood pressure, and temperature. • **Dose Modification:** See tables 1 and 2 • Maximum cumulative dose of daunorubicin = 600mg/m^2. Check previous exposure to anthracyclines. • Central line required for daunorubicin infusion, otherwise Daunorubicin could be given as bolus via peripheral line.
References	SPC accessed 16/04/2019 North West London cancer alliance trial protocol AML-17v1l KMCC SACT protocol HAEM-AML-029v1 MYLOTARG® (gemtuzumab ozogomicin) Licensed Dosage Schedule Pfizer MI

NB For funding information, refer to the SACT funding spreadsheet

Table 1

Dose modifications for haematological toxicities

Haematological toxicities	**Dose modifications**
Persistent thrombocytopenia (Platelets < 100,000/mm^3 at the planned start date of the consolidation course)	• Postpone start of consolidation course. • If platelet count recovers to ≥ 100,000/mm^3 within 14 days following the planned start date of the consolidation course: initiate consolidation therapy • If platelet count recovers to < 100,000/mm^3 and ≥ 50,000/mm^3 and within 14 days following the planned start date of the consolidation course: gemtuzumab should not be re-introduced and consolidation therapy should consist of DNR and AraC only. • If platelet count recovery remains < 50,000/mm^3 for greater than 14 days, takes longer than 14 days, or if platelet count does not recover to ≥ 50,000/mm^3 consolidation therapy should be re-evaluated and a BMA should be performed to re-assess the patients' status.
Persistent neutropenia	• If neutrophil count does not recover to > 500/mm^3 within 14 days following the planned start date of the consolidation cycle (14 days after haematologic recovery following previous cycle), discontinue gemtuzumab (do not administer gemtuzumab in the consolidation cycles).
Abbreviations: AML=acute myeloid leukaemia; AraC=cytarabine; BMA=bone marrow aspirate, DNR=daunorubicin.	

Table 2

Dose modifications for non-haematological toxicities

Non-haematological toxicities	**Dose modifications**
VOD/SOS	Discontinue gemtuzumab ozogamicin
Total bilirubin > 2 × ULN and AST and/or ALT > 2.5 × ULN	Postpone gemtuzumab ozogomicin until recovery of total bilirubin to ≤ 2 × ULN and AST and ALT to ≤ 2.5 × ULN prior to each dose. Consider omitting scheduled dose if delayed more than 2 days between sequential infusions.
Infusion related reactions	Interrupt the infusion and institute appropriate medical management based on the severity of symptoms. Patients should be monitored until signs and symptoms completely resolve and infusion may resume. Consider permanent discontinuation of treatment for severe or life-threatening infusion reactions.
Other severe or life-threatening non-haematologic toxicities	Delay treatment with gemtuzumab until recovery to a severity of no more than mild. Consider omitting scheduled dose if delayed more than 2 days between sequential infusions.
Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; SOS=sinusoidal obstruction syndrome; ULN=upper limit of normal; VOD=venoocclusive disease.	

Induction Cycle 1

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Chlorphenamine	10mg	IV	stat	1 hour before gemtuzumab ozogamicin
	Paracetamol	1000mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Dexamethasone	8mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Ondansetron	8mg	PO		BD
	GEMTUZUMAB OZOGAMICIN	**3 mg/m2 (max. 5mg vial)**	IV	2 hours	Dilute in 50ml sodium chloride 0.9% (or to a concentration between 0.075 mg/ml to 0.234 mg/ml) Doses < 3.9mg must be administered by syringe. Protect from light. Administer with in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter.
	DAUNORUBICIN	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
Day 1-7	**CYTARABINE**	**1400mg/m^2/7 days** **(ie 200mg/m^2/day for 7 days)**	IV	Cont. infusion	To be given via a continuous infusion pump over 7 days.
Day 2	Ondansetron	8mg	PO		BD
	DAUNORUBICIN	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
Day 3	Ondansetron	8mg	PO		BD
	DAUNORUBICIN	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion

Day 4	Chlorphenamine	10mg	IV	stat	1 hour before gemtuzumab ozogamicin
	Paracetamol	1000mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Dexamethasone	8mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Ondansetron	8mg	PO		BD
	GEMTUZUMAB OZOGAMICIN	**3 mg/m^2 (max. 5mg vial)**	IV	2 hours	Dilute in 50ml sodium chloride 0.9% (or to a concentration between 0.075 mg/ml to 0.234 mg/ml) Doses < 3.9mg must be administered by syringe. **Protect from light.** Administer with in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter.
Day 5	Ondansetron	8mg	PO		BD
Day 6	Ondansetron	8mg	PO		BD
Day 7	Chlorphenamine	10mg	IV	stat	1 hour before gemtuzumab ozogamicin
	Paracetamol	1000mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Dexamethasone	8mg	PO	stat	1 hour before gemtuzumab ozogamicin
	Ondansetron	8mg	PO	stat	BD
	GEMTUZUMAB OZOGAMICIN	**3 mg/m2** **(max. 5mg vial)**	IV	2 hours	Dilute in 50ml sodium chloride 0.9% (or to a concentration between 0.075 mg/ml to 0.234 mg/ml) Doses < 3.9mg must be administered by syringe. Protect from light. Administer with in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter.

Induction Cycle 2

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	2 hours	In 500ml 0.9% sodium chloride
	DAUNORUBICIN	**35mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
	Ondansetron	8mg	PO		stat **to be given 12 hours after first dose**
	CYTARABINE	**1000mg/m²**	IV	2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 2	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	2 hours	In 500ml 0.9% sodium chloride
	DAUNORUBICIN	**35mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
	Ondansetron	8mg	PO	stat	stat **to be given 12 hours after first dose**
	CYTARABINE	**1000mg/m²**	IV	2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 3	Ondansetron	8mg	PO		BD **12 hours apart**
	CYTARABINE	**1000mg/m²**	IV	2 hours	BD **12 hours apart** In 500ml 0.9% sodium chloride

If the patient has attained complete remission, gemtuzumab ozogamicin should be continued in up to 2 cycles of consolidation chemotherapy.

Consolidation Cycle 1

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Chlorphenamine	10mg	IV	stat	1 hour before gemtuzumab ozogamicin
	Paracetamol	1000mg	PO		1 hour before gemtuzumab ozogamicin
	Dexamethasone	8mg	PO		1 hour before gemtuzumab ozogamicin
	Ondansetron	8mg	PO		stat
	GEMTUZUMAB OZOGAMICIN	**3 mg/m2 (max.5mg vial)**	IV	2 hours	Dilute in 50ml sodium chloride 0.9% (or to a concentration between 0.075 mg/ml to 0.234 mg/ml) Doses < 3.9mg must be administered by syringe. **Protect from light.** Administer with in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter.
	CYTARABINE	**1000mg/m²**	IV	2 hours	In 500ml 0.9% sodium chloride
	DAUNORUBICIN	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
	Ondansetron	8mg	PO		stat to be given 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 2	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride

Day 2 cont	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 3	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 4	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride

Consolidation Cycle 2:

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Chlorphenamine	10mg	IV	stat	1 hour before gemtuzumab ozogamicin
	Paracetamol	1000mg	PO		1 hour before gemtuzumab ozogamicin
	Dexamethasone	8mg	PO		1 hour before gemtuzumab ozogamicin
	Ondansetron	8mg	PO		stat
	GEMTUZUMAB OZOGAMICIN	**3 mg/m2 (max. 5mg vial)**	IV	2 hours	Dilute in 50ml sodium chloride 0.9% (or to a concentration between 0.075 mg/ml to 0.234 mg/ml) Doses < 3.9mg must be administered by syringe. **Protect from light.** Administer with in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter.
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride
	DAUNORUBICIN	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 2	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride

Day 2 cont	**DAUNORUBICIN**	**60mg/m²**	IV	30 mins	Dilute in sodium chloride 0.9% 100ml-250ml or undiluted via a fast running sodium chloride 0.9% infusion
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 3	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride
Day 4	Ondansetron	8mg	PO		stat
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours	In 500ml 0.9% sodium chloride
	Ondansetron	8mg	PO		Stat 12 hours after first dose
	CYTARABINE	**1000mg/m²**	IV	Over 2 hours **To be given 12 hours after first dose**	In 500ml 0.9% sodium chloride

TTO MEDICATION (all cycles unless specified)	**Drug**	**Dose**	**Route**	**Directions**
	Chlorhexidine mouthwash	10ml	MW	Four times daily for 4 weeks OR stop after neutrophils > 1.0
Cycle 1 only	Allopurinol	300mg	PO	Once daily. Review after 4 weeks. Adjust dose in renal impairment.
	Aciclovir	400mg	PO	Twice daily for 4 weeks
Induction cycle 2 Consolidation Cycle 1 & 2	Prednisolone 0.5% eye drops	1 drop	to both eyes QDS	Starting on Day 1 of cycle for 7 days.
	Metoclopramide	10mg	PO	TDS for 3 days after the end of each cycle of chemo then 10mg TDS PRN. Do not take for more than 5 days continuously.
Induction cycle 2 only	Dexamethasone	6mg	PO	OM from **day 4** for 3 days on induction cycle 2 only.
Consolidation Cycle 1&2 only	Dexamethasone	6mg	PO	OM from **day 5** for 3 days on consolidation cycles only.
	Prescribe anti-fungals			