Clinical Trials Summary for out of hours Important Reference

Lancashire Teaching Hospitals NHS Foundation Trust

Acronym study title	**Shattuck Labs SL03-OHD-105**
Study Details	An Open-Label, Phase 1b Study of SL-172154 (SIRPα-Fc-CD40L) Administered with Either Pegylated Liposomal Doxorubicin or Mirvetuximab Soravtansine in Subjects with Platinum-Resistant Ovarian Cancers
Principal Investigator PI Sub PI's	**PI –** Dennis Hadjiyiannakis (Dennis.Hadjiyiannakis@lthtr.nhs.uk) **Sub Investigator -** David Cameron (David.Cameron@lthtr.nhs.uk)
Research Nurse Team	**Senior Research Nurse Karen Jones** (Karen.Jones4@lthtr.nhs.uk) **Research Nurse –** Elizabeth Coates
Drug therapy	This study involves treating patients with Ovarian cancer with SL-172154 (given in 3/4 weekly cycles) in combination with Doxorubicin or Mirvetuximab. The IMP, SL-172154, is a fusion protein with two effects: checkpoint blockade (CD47) in combination with tumor necrosis factor activation (CD40). PLD (Doxorubicin) is a commonly used chemotherapy drug. See local guidelines for safety profile and management. Mirvetuximab Soravtansine (MIRV) is an anti-folate receptor alpha antibody/drug conjugate. <u>Adverse Events</u> Most common drug-related IMP AEs (>15%): Infusion Related Reaction (60.9%) Fatigue (39.1%) Nausea (17.4%) Less commonly reported Aes Constipation (21.7%) not drug related Grade 3 ALT increased (4.3%) drug related Grade 3 AST increased (4.3%) drug related Grade 3 Anaemia (4.3%) drug related Dysesthesia (4.3%) Jaw pain (4.3%) Vision blurred (4.3%) COVID-19 (4.3%)

	Decreased Appetite (4.3%) Diarrhea (4.3%) Dyspnoea (4.3%) MIRV AEs reported in patients treated with MIRV: Nausea (46% all grades; 1% Grade ≥3) Vomiting (16% all grades; 1% Grade≥3) Mild to moderate diarrhoea Noninfectious Pneumonitis Neutropenia Thrombocytopenia Ocular Disorders (Dry-eye, Keratopahy, Blurred Vision, Eye pain, Photophobia). **All patients receiving MIRV will be under the review of an Ophthalmologist** <u>IMP Severe Adverse Events reported</u> Embolism 8.7% - not related to IMP Sepsis 8.7% - not related to IMP Lower GI haemorrhage 4.3% - not related to IMP SB Obstruction 4.3% - not related to IMP Worsening muscle weakness of lower limb 4.3% **<u>Infusion related reactions</u>** Infusion related reactions or Cytokine Release Syndrome (CRS) are possible events in this study. Patients complaining of fever post infusion should be assessed for possible CRS. The Sponsor have been asked to cover the cost of Tocilizumab in case needed.
In the event that a patient calls this hotline for advise	Refer to SoC protocol for additional information regarding Doxorubicin treatment. Advise patient to seek medical assistance via nearest available healthcare provider depending upon severity of symptoms. Advise patient to keep all relevant trial paperwork with them for review by treating clinician. Patients requiring admission may be reviewed by the on-call Oncology SpR/Consultant. If escalation is required, please alert PI/Co-I on the above emails or 01772 522031. Treatment interruption/modification may be required.

3.7.1.5 Management of Other AEs Not Specified

Severity	Dose Modification	Toxicity Management
All Grades	Note: Dose modifications are not required for AEs not deemed to be related to SL-172154 (i.e., events due to underlying disease) or for laboratory abnormalities not deemed to be clinically significant.	• Treat accordingly, as per institutional standard
Grade 1	No dose modification required.	• Treat accordingly, as per institutional standard
Grade 2	Consider reducing the SL-172154 by one dose level or holding SL-172154 until resolution to ≤Grade 1 or baseline.	• Treat accordingly, as per institutional standard
Grade 3	Hold SL-172154 until resolution to ≤Grade 1 or baseline. For AEs that downgrade to ≤Grade 2 within 7 days or resolve to ≤Grade 1 or baseline within 14 days, resume SL-172154 at one dose level lower. Otherwise, discontinue SL-172154. (Note: For Grade 3 labs, decision to hold should be based on accompanying clinical signs/symptoms, the Investigator's clinical judgment, and consultation with the Sponsor).	• Treat accordingly, as per institutional standard
Grade 4	Permanently discontinue SL-172154. (Note: For Grade 4 labs, decision to discontinue should be based on accompanying clinical signs/symptoms, the Investigator's clinical judgment, and consultation with the Sponsor).	• Treat accordingly, as per institutional standard

3.7.3.2 Dose Modifications for MIRV-Related Adverse Events

Table 7 Dose Modifications for MIRV-related Adverse Events

Severity Grade (CTCAE v5.0)	Dose Modifications for MIRV[a]
HEMATOLOGICAL	
Neutropenia	
Grade 2 and Grade 3	Hold drug until ANC is ≥1.5 x10^9/L (1500/µL) and resume at the same dose level
Grade 4	Hold drug until ANC is ≥1.5 x10^9/L (1500/µL) and then resume at one lower dose level
Febrile neutropenia Grade 3 or 4 (with single temperature reading ≥38.3°C or a sustained temperature of >38°C for >1 hour)	Hold drug until ANC is ≥1.5 x10^9/L (1500/µL) and then resume at one lower dose level

Severity Grade (CTCAE v5.0)	Dose Modifications for MIRV[a]
Thrombocytopenia	
Grade 2 and Grade 3	Hold drug until PLT count is ≥100 x 10^9/L (100,000/µL) and resume at same dose level
Grade 3 associated with clinically significant bleeding that requires transfusion therapy Grade 4	Hold drug until PLT count is ≥100 x 10^9/L (100,000/µL) and resume at same dose level
NON-HEMATOLOGICAL	
Nausea and Vomiting	
Grade 3 (despite use of optimal antiemetics)	Hold drug until resolved to Grade ≤1, then resume at one lower level
Grade 4	Permanently discontinue
Diarrhea	
Grade 3 (despite use of optimal antidiarrheal treatment)	Hold drug until resolved to Grade ≤1, then resume at one lower level
Grade 4	Permanently discontinue
Ocular Disorders	Refer to Section 3.7.3.5
Non-infectious Pneumonitis	Refer to Section 3.7.3.6
Infusion-related Reactions (IRR)	Refer to Section 3.7.3.8
ALL OTHER NON-HEMATOLOGICAL TOXICITIES (except AEs related to underlying disease, Grade 3 fatigue, isolated symptomatic Grade 3 biochemistry laboratory abnormalities that last for <7 days including electrolyte abnormalities that respond to medical intervention)	
Grade 3	Hold drug until resolved to Grade ≤1, then resume at one lower level For any Grade 3 hepatic toxicity that does not resolve to baseline within 7 days, an abdominal CT scan must be performed to assess whether it is related to progressive disease.
≥Grade 3 cardiac events (excluding Grade 3 hypertension)	Permanently discontinue
Grade 4	Permanently discontinue

Abbreviations: AE = adverse event; ANC = absolute neutrophil count; CT = computed tomography; CTCAE = common terminology criteria for adverse events; MIRV = mirvetuximab soravtansine; PLT = platelets.