TABLE 2: Medication treatment options and recommendations by complex lymphatic anomaly

MEDICATION	INDICATION	DIAGNOSES	INITIAL DOSE/ REGIMEN	LENGTH OF THERAPY	POTENTIAL COMPLICATIONS†
Sirolimus	Bone lytic lesions Effusions LM engorgement Pain	GLA GSD KLA CCLA††	0.8mg/m^2/dose PO every 12 hours* Trough target level: 8-12ng/mL	Indefinite OR transition to other targeted therapy	Oral mucositis High triglycerides Immunosuppression (consider PJP prophylaxis)
Interferon alpha 2b	Bone lytic lesions Effusions	GLA GSD KLA	Pegylated form: 1.5mcg/kg/dose subQ weekly	Indefinite (but may be limited due to complications)	Flu-like symptoms with administration Hypothyroidism
Vincristine	Coagulopathy Effusions	KLA	>10kg: 1.5mg/ m^2/dose IV weekly initially, max 2mg/dose ≦10 kg: 0.05mg/kg/dose	Taper off as coagulopathy improves	Peripheral neuropathy Constipation Bone pain SIADH Extravasation risk Hair loss
Steroids	Coagulopathy Effusions	KLA	Methylprednisone IV 1.6mg/kg/day OR Prednisolone PO 2mg/kg/day, initially	Taper off over 2-3 months if possible	Hyperglycemia Increased appetite Stomach/duodenal ulcers Weight change Mood/sleeping disturbances
Zoledronic acid	Bone lytic lesions Pathogenic fractures	GLA GSD KLA	VAC: 0.05 mg/kg/dose IV every 6 months, max 4mg/dose	2 years max	Infusion reactions (including anaphylaxis) Osteonecrosis of jaw Electrolyte disturbances Atypical femur fracture
			HVMC: 4mg/m^2/dose IV monthly x 3 doses, then every 3 months, max 4mg/dose	Reassess need after 10 doses 5 years max	
Trametinib	Bone lytic lesions Effusions Coagulopathy (KLA)	KLA CCLA††	0.025mg/kg/dose PO once daily, max 2mg/dose** 0.5mg, 1mg, 2mg tablets available only	Indefinite OR transition to other targeted therapy	Skin rash Edema Diarrhea Increased liver enzymes Hair lightening or loss Oral mucositis

Abbreviations: CCLA, central conducting lymphatics anomaly; HVMC, Hemangioma and Vascular Malformation Center at Cincinnati Children's Hospital Medical Center; GLA, generalized lymphatic anomaly; GSD, Gorham-Stout Disease; IV, intravenously; KLA, kaposiform lymphangiomatosis; LM, lymphatic malformation; PJP, *Pneumocystis jirovecii* pneumonia; PO, per oral; SIADH, syndrome of inappropriate antidiuretic hormone secretion; subQ, subcutaneously; VAC, Vascular Anomalies Center at Texas Children's Cancer and Hematology Centers.
†Common and notable lesser common complications listed. This is not an extensive list of all potential side effects.
††Response to disease-modifying agents such as sirolimus and trametinib for CCLA is unclear. *EPHB4* mutation recently found in CCLA suggests there may be a role for mTOR or MAPK/MEK inhibition.
*Dosing for infants and young children is different due to metabolism differences. Recommended dosing for infants and young children under 2 years of age is based on pharmacokinetic studies by Mizuno et al. [32]
**Suggested dosing based on clinical trials of trametinib use in children with plexiform neurofibromas and gliomas.