

**CONCEPT G: Concept Sheet for a Potential Trial Addressing an Unresolved Issue in Osteosarcoma**

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<b>Short title</b>	<b>[G]</b> Pulmonary metastasectomy +/- systemic therapy for lung-only metastatic osteosarcoma
<b>Summary diagram</b>	(See end of document)
<b>Patient group (Summary only)</b>	Lung-only metastatic osteosarcoma
<b>Main eligibility criteria (Summary only)</b>	Lung-only metastatic osteosarcoma with potentially resectable lung metastases
<b>Control treatment (Name, administration route, duration)</b>	Pulmonary metastasectomy alone
<b>Research treatment(s) (Name, administration route, duration)</b>	Systemic therapy (to be determined) given either pre or post-operatively or both
<b>Current knowledge (Known safety data and known activity data)</b>	The options are to use standard chemotherapy regimens or include novel agents
<b>Rationale (250 words max)</b>	Without treatment most patients with metastatic sarcoma die within one year. The current surgical treatment of pulmonary metastases from bone and soft tissue sarcoma has evolved based on weak evidence from retrospective cohort studies. These studies have shown that pulmonary metastasectomy (PM) achieves 5 year overall survival rates of 30-40% and it is now considered the standard of care in patients with potentially resectable lung metastases. Peri-operative chemotherapy given at the time of PM has been shown to improve survival in some studies but not others. The timing of chemotherapy in relation to surgery (pre or post-operative) and the type of drugs administered varies at institutions throughout the world. Factors taken into consideration include the time from primary diagnosis to the development of metastases and the timing and nature of prior systemic agents. The optimal type of systemic therapy and its timing in relation to PM is unknown.
<b>Hypothesis (50 words max)</b>	Systemic therapy in combination with PM will improve overall survival in patients with lung-only metastases from osteosarcoma. Prognostic factors influencing survival in these patients will include disease free interval from primary diagnosis and the number and size of lung metastases.
<b>Trial design</b>	Phase I

		non-randomised Phase II, specify: _____
		randomised phase II, specify: _____
	X	Phase III
<b>Blinding</b>		Single blinding possible
		Double blinding possible
	X	No blinding possible
<b>Primary outcome measure</b>	Overall survival	
<b>Secondary outcome measures</b>	<ul style="list-style-type: none"> <li>-Progression free survival (for patients treated with systemic therapy pre-operatively)</li> <li>-Relapse free survival (for patients treated with systemic therapy post-operatively)</li> <li>-Response rate of systemic therapy given pre-operatively</li> <li>-Toxicity of systemic therapy</li> <li>-Surgical adverse events</li> <li>-Quality of life measured by QLQ-C30 and QLQ LC13</li> <li>-Time without symptoms of disease or toxicity of treatment (Q-TWIST).</li> <li>-Potential for biological/translation sub-studies</li> </ul>	
<b>Control arm event rate</b>	40 % events at 5 years	
<b>Accrual duration</b>	5 years	
<b>Accrual rate / year</b>	100 patients / year	
<b>Accrual total target</b>	500 patients	
<b>Total trial duration</b>	10 years	
<b>Need for international collaboration</b>	Yes	
<b>Potential sub-studies</b>	X	Biology / translation
	X	Quality of life
		Other, specify: _____

Summary diagram

