CLINICAL PRIORITIES ADVISORY GROUP
06 and 07 November 2018

Agenda Item No	04.2
National Programme	Cancer
Clinical Reference Group	Radiotherapy
URN	170102P

Title
Selective internal radiation therapy (SIRT) for chemotherapy refractory / intolerant metastatic colorectal cancer (Adults).

Actions Requested	1. Support the adoption of the policy proposition
	2. Recommend the relative prioritisation

Proposition
The policy proposition recommends that selective internal radiation therapy (SIRT), a form of radiotherapy, be routinely commissioned for the treatment of adults with chemotherapy refractory / intolerant metastatic colorectal cancer where the spread of the colorectal cancer is limited to the liver. SIRT is an alternative treatment to best supportive and/or palliative care. The aim of SIRT is to control the growth of the cancer but it is not curative. The policy proposition also includes treatment eligibility criteria which are based on the available clinical evidence and include that the cancer must not be amenable to surgical resection and that there must be five or fewer tumours within the liver affecting ≤25% of the total liver volume. SIRT was previously available via a Commissioning through Evaluation (CtE) scheme which closed in 2017. The policy proposition has been developed following consideration of both the CtE findings, together with two new Evidence Reviews which cover the different types of radioactive agents used in SIRT treatments (Yttrium-90 and Holmium-166).

Clinical Panel recommendation
The Clinical Panel recommended that the policy progress as a routine commissioning policy.

The committee is asked to receive the following assurance:	
1.	The Head of Clinical Effectiveness confirms the proposal has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report
2.	The Head of Acute Programmes confirms the proposal is supported by an: Impact Assessment; Stakeholder Engagement Report; Consultation Report; Equality Impact and Assessment Report; Clinical Policy Proposition. The relevant National Programme of Care Board has approved these reports.
3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.
4.	The Operational Delivery Director (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Proposition
2.	Consultation Report
3.	Evidence Summary
4.	Clinical Panel Report
5.	Equality Impact and Assessment Report

The Benefits of the Proposition – Use of SIRT to treat unresectable, chemotherapy refractory liver dominant metastatic colorectal carcinoma versus best supportive care		
No	*Outcome measures*	*Summary from evidence review*
1.	Survival	*Ytrrium-90 microsphere data from retrospective matched comparative study; Seidensticker et al., 2012* There was a significant survival benefit for patients treated with SIRT (median of 8.3 months) compared to best supportive care (median of 3.5 months); sample size: 29 patients in SIRT group and 29 in best supportive care (BSC) group. 2 retrospective studies provided overall survival data; both of which are subject to a high risk of bias which may impact on the reliability of outcomes. *Yttrium-90 microsphere data from Commissioning Through Evaluation Project – SIRT registry study (non-comparative).*

		Median overall survival was 7.6 months (95% CIs 6.9-8.3) and survival at 12 months following SIRT was 30%. Subgroup analyses showed that absence of extrahepatic disease, fewer liver tumours, smaller tumour to liver volume percentage, and being male, were factors associated with a survival benefit. Median overall survival figures for patients in subgroups without extrahepatic disease are: • 1 to 5 tumours – 11.3 months (95% CIs 8.1-14.5); • Tumour to liver volume ≤25% - 9.7 months (95% CIs 7.4-11.9); • Both 1 to 5 tumours and tumour to liver volume ≤25% - 12.9 months (95% CIs 9.1-16.6). *Holmium-166 microsphere data from non-comparative study; Prince et al., 2017* Median survival for patients with colorectal cancer was 13.4 months after treatment with SIRT with holmium-166. However, this was not compared with best supportive care and so 'survival benefit' cannot be determined.
2.	Progression free survival	*Ytrrium-90 microsphere data from retrospective matched comparative study; Seidensticker et al., 2012* Progression free survival (PFS) may be longer in patients treated with SIRT compared with BSC SIRT; however a statistical comparison was not carried out. This study is subject to a high risk of bias which may impact on the reliability of outcomes. *Yttrium-90 microsphere data from Commissioning Through Evaluation Project – SIRT registry study (non-comparative).* Median progression-free survival was 3.0 months (95% CIs 2.8-3.1) and median liver-specific progression-free survival was 3.7 months (95% CIs 3.2-4.3).
3.	Mobility	Not measured
4.	Self-care	Not measured
5.	Usual activities	Not measured
6.	Pain	Not measured
7.	Anxiety / Depression	Not measured
8.	Replacement of more toxic treatment	Not measured

9.	Dependency on care giver / supporting independence	Not measured
10.	Safety	*Ytrrium-90 microsphere data from retrospective matched comparative study; Seidensticker et al., 2012* Treatment-related adverse events following SIRT included: in the first 14 days post-SIRT grade 1–2 fatigue (n = 20, 69%), grade 1 mild abdominal pain/nausea (n = 14, 48.3%), and grade 2 gastrointestinal ulceration (n = 3, 10.3%). There were 3 cases (10.3%) of grade 3 radiation-induced liver disease not deemed life-threatening. Adverse events were not reported for the BSC group. 2 retrospective studies provided data on adverse events neither of which reported adverse events for their supportive care groups and both are subject to a high risk of bias. *Yttrium-90 microsphere data from Commissioning Through Evaluation Project – SIRT registry study (non-comparative).* Severe complications on the day of treatment were reported in 11 patients (3%). During the follow-up period, 36% of patients experienced an adverse event, of which 8% of the events were grade 3 and above (severe). The most frequently reported adverse events were mild fatigue and abdominal pain. *Holmium-166 data from non-comparative study; Prince et al., 2017* Adverse events data were collected. However, these were not stratified by primary cancer diagnosis and so results for patients with colorectal cancer cannot be reported.
11.	Delivery of intervention	Not measured

Other health outcome measures determined by the evidence review		
No	Outcome measure	Summary from evidence review
1.	Cost-effectiveness	*Ytrrium-90 microsphere data from cost-effectiveness analysis; Pennington et al., 2015* When comparing SIRT to best supportive care (BSC)

		results indicated that SIRT is potentially cost-effective with an incremental cost effectiveness ratio (ICER) of £28,216. The data used to obtain the cost-estimate is subject to bias and some model assumptions and inputs that were used may not be appropriate which may impact on the reliability of the cost estimate of SIRT. *Yttrium-90 microsphere data from Commissioning Through Evaluation Project – SIRT registry study (non-comparative).* The ICER for SIRT compared to best supportive care was £85,350 in the base case. Treatment with SIRT resulted in an increase in QALYs of 0.32 (0.58 vs 0.26). The model showed that SIRT was £27,406 more expensive than best supportive care (£31,028 vs £3,623 discounted costs). This was primarily due to high initial procedure costs in the SIRT arm. The cost of the SIRT procedure and the survival time were the main drivers in the model. Scenario analysis where a longer survival estimate and a lower procedure cost were used with a longer time horizon, based on the published model by Pennington et al. (2015), resulted in a lower ICER of £31,888. This demonstrates the impact of the overall survival and the procedure cost on the model outcomes.
1.	Quality of life	*Yttrium-90 microsphere data from Commissioning Through Evaluation Project – SIRT registry study (non-comparative).* Health related quality of life measured using EQ-5D-5L and EQ-VAS remained relatively high and constant before and after the SIRT procedure. A statistically significant reduction in health related quality of life was observed 3 months following SIRT but this was small and not clinically relevant. No significant change was observed at 6 and 9 months, although the number of respondents was small. *Ytrrium-90 microsphere data from cost-effectiveness analysis; Pennington et al., 2015* *When comparing SIRT to best supportive care (BSC) results indicated that SIRT is potentially cost-effective with an incremental cost effectiveness ratio (ICER) of £28,216.* *The data used to obtain the cost-estimate is subject to bias and some model assumptions and inputs that were used may not be appropriate which may impact on the reliability*

		of the cost estimate of SIRT.

Considerations from review by Rare Disease Advisory Group
Not applicable.

Pharmaceutical considerations
Not applicable.

Considerations from review by National Programme of Care
The proposal received the full support of the Cancer PoC Board on 28th September 2018.