CIRT CIRSE Registry for SIR-Spheres Therapy

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Study objectives

Primary end point

The primary objective is to observe the real-life clinical application of SIRT with SIRT Y-90 resin microspheres and the impact of the treatment in clinical practice. This will be categorized as one of the following 5 categories with sub-categories:

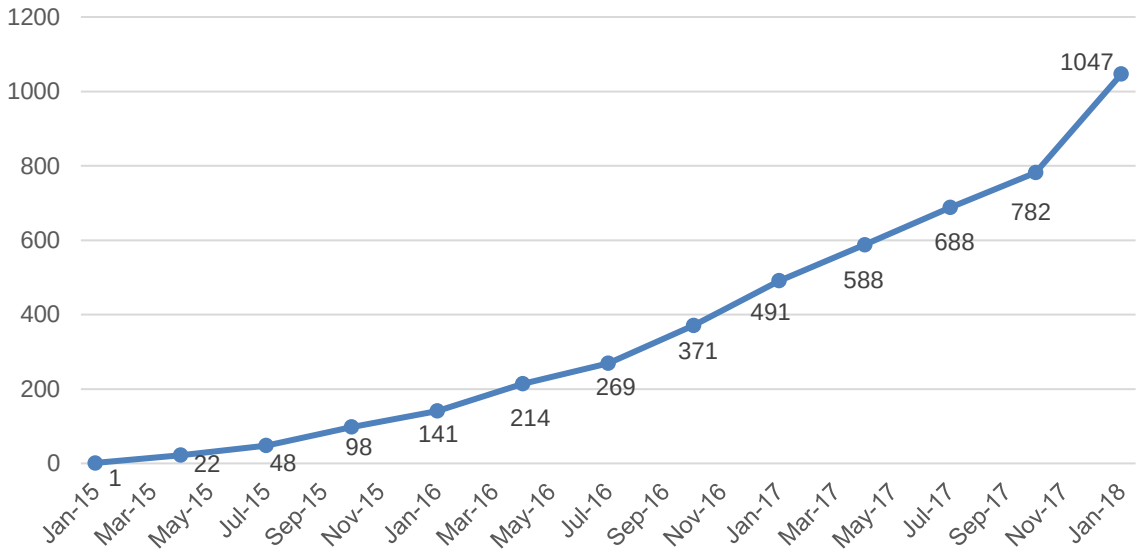
1. Type of liver cancer (primary or secondary/metastatic)
2. Intention of treatment (bridging, down-sizing, palliative or ablation)
3. Prior hepatic procedures (surgical, ablative, vascular and abdominal)
4. Associated systemic therapy (prior- and post-SIRT systemic therapy and concomitant chemotherapy)
5. Post-SIRT hepatic procedures (surgical, ablative, vascular and abdominal)

Study objectives

Secondary end points

Effectiveness	Overall survival Progression-free survival Hepatic progression-free survival Imaging response
Safety	Treatment complications Adverse events Laboratory assessments
Technical considerations	Patient-related characteristics Treatment planning Treatment administration Procedure-related outcomes
Quality of life	QLQ-C30 with HCC Module (if HCC)

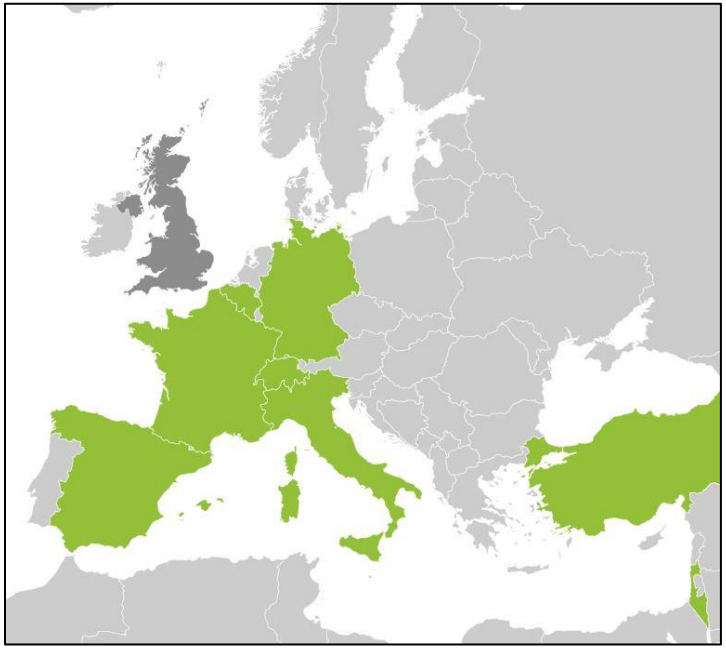
Enrolment figures



Patient distribution per country

- 8 countries
- 27 hospitals
- 1047 patients

Country	Hospitals	Patients
Belgium	4	100
France	1	58
Germany	12	424
Israel	1	14
Italy	5	176
Spain	1	32
Switzerland	1	120
Turkey	2	123



How did we get there: baseline

Status quo in 2013

- BSIR SIRT registry in the UK just started with patient enrolment
  - Commissioned by the National Institute for Health and Care Excellence (NICE) as a service evaluation of the use of SIRT in routine care in the UK
  - Already enrolling patients
  - Ready-to-go electronic data capturing system (EDC) and case report form (CRF)
  - CIRSE could adopt and adapt this system to its own needs

- SIRTEX was the clear market leader in radioembolisation at the time and an observational study on SIR-Spheres would reflect well how radioembolisation is performed in Europe, thus justifying a single device study

- No large data sets existed on the clinical application of SIRT in Europe

How did we get there: the first steps

Original purpose of the study

Exploratory

- No large-scale body of evidence existed on how SIRT was performed in European clinics
- Possibilities to find potential relationships between indications, treatment modalities and outcomes

Inclusive

- All indications
- As many countries as possible
- As much data as feasible

First CIRT objective

"The objective of CIRT is to prospectively capture as broad a spectrum of data as feasible, with the aim of understanding the real-life application of radioembolisation with SIR-Spheres microspheres. Due to the observational nature of CIRT the investigators decided not to predefine detailed research questions and therefore specific endpoints" (CIRT Protocol, 27 October 2014)

Progression to maturity: a critical evaluation

- CIRT actually started to be more successful than anticipated
  - More hospitals interested than expected
  - Progressive patient enrolment
- Realisation that CIRT data has a lot of value and potential

- Refining the science:
  - Coming to a concrete definition of “real-life application”
  - Review and refine the CRF to ensure all data is captured and objectives are met
  - Concrete measurements for safety, effectiveness and quality of life
  - Develop a statistical analysis plan with an independent statistician

- Rethinking the research infrastructure – ensuring quality control

Developing the research infrastructure

CIRSE Study SOPs

- Defining clear SOPs for
  - Site invitations and contracting
  - Remote monitoring and data quality control

EDC

- Critically evaluate the electronic data capturing (EDC) system against industry standards
  - No reliance on third-party programming, ability to modify data points when needed
  - Ability to control levels of authorisation (CIRT can only include PIs. PIs responsible for including local users)
  - Direct site interaction through EDC interface

Learn to evaluate local resources and qualifications

- Not all sites have a study centre or study nurses
- Rely on information from sites instead of industry regarding treatment volume

CIRT: summary

Strengths	Points for development	Solutions
• Large data sample (+1000) • Inclusive (all indications) • 150+ data points per patient and high data completion • Many publications and congress presentations possible • Multidisciplinary Steering Committee	• Poorly defined objectives at the beginning of the study • Poor understanding of site infrastructure and needs • Poor EDC • No system for quality control • One IR chairperson, missing the perspective of other relevant disciplines for day-to-day decision-making	• Objectives reworked throughout the study • Qualification questionnaire for site initiation • Now OpenClinica for future studies • CIRSE Quality System • Dual Chairpersonship, multidisciplinary

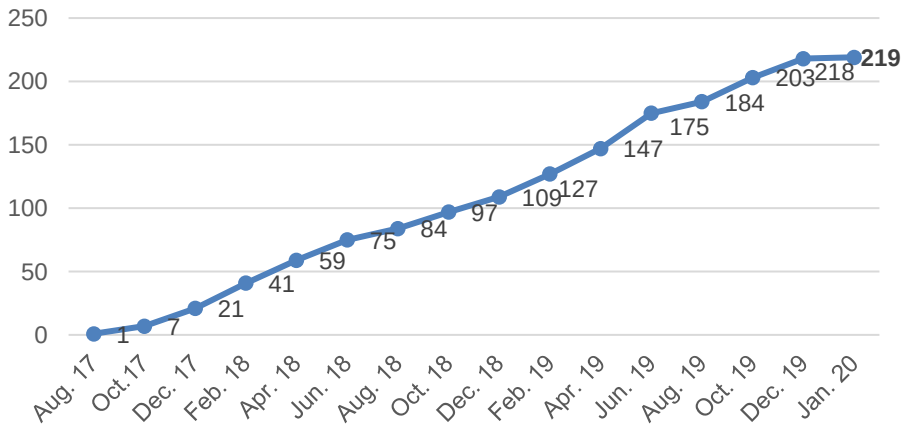
Implementing lessons learned: CIRT-FR

Reimbursement study

- Commissioned by the French national health authorities (HAS) to evaluate the clinical application and outcomes from SIR-Spheres following approval of reimbursement for patients with mCRC in March 2017
- Working to external standards: reviewed and approved by French governmental institutions (HAS, CNIL, CDEDiMTS)
- Using the verified primary and secondary end points from CIRT
- Proof of concept that CIRSE can successfully initiate and conduct reimbursement studies

Implementing lessons learned: CIRT-FR

Patient enrolment: August 2017 – January 2020 (n=219)



Improvements compared to CIRT

- Well-defined objectives and CRF
- Full deployment of CIRSE Quality System for data monitoring
- Involvement of study nurses and study centres from the beginning
- Inclusion of case logs to understand patient representation (96%)
- Dual chairpersonship: Prof. Thomas Helmberger and Prof. Valérie Vilgrain

Thank you!

CIRT & CIRT-FR Steering Committee CIRSE 2019