CIEMAR

CIRSE Emprint Microwave Ablation Registry

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Rationale for CIEMAR and value of information – scarcity of robust data

- Although there are numerous observational studies and case series on thermal ablation modalities for CRLM, robust research to assess its effectiveness is lacking, in particular in the case of the newest technology MWA.
- The CLOCC trial marks a notable exception, although it too has to be interpreted carefully due to the study being underpowered and a significant part of the ablation arm also having received a partial Hepatectomy.
- Nevertheless, the substantial difference in 8-year OS (8.9% versus 35.9%) and 8-year disease-free survival (22.3% versus 2.0%) justified the adoption of thermal ablation for unresectable CRLM.
- CIEMAR ultimately seeks to
  - substantiate the evidence base for the effectiveness and safety of thermal ablation of CRLM in a large-scale, multi-centric, cross-border sample
  - extend the current evidence base regarding MWA with appropriately defined follow-up data, as well as data regarding quality of life and cost effectiveness

Study objectives - Primary

Primary objective

To assess the effectiveness and safety of microwave ablation performed with the Emprint device in controlling colorectal metastatic tumours in the liver.

Patient target: 1000 patients, to be recruited from 72 invited sites by 2025, 2 years site enrolment + 3 years follow-up

Primary endpoint

Primary efficacy endpoint	Outcome measure
Efficacy	Local tumour control at 12 months following MWA on a per-lesion basis

Primary safety endpoint	Outcome measure
Safety	Frequency and severity of adverse events and toxicity (CTCAE V5.0)

Study objectives - Secondary

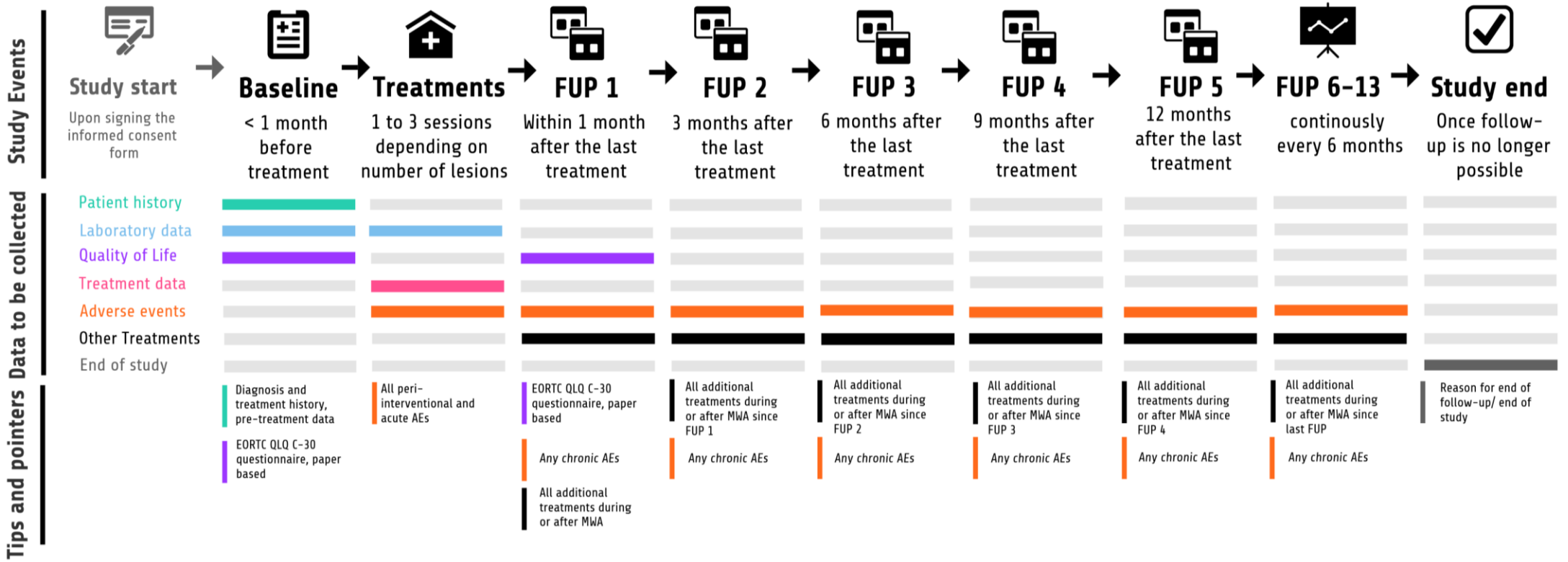
Secondary objectives

Evaluate survival, efficacy parameters, quality of life and economic aspects of MWA for liver metastases.

Secondary endpoints

Efficacy	Overall survival Overall disease-free survival Hepatic disease-free survival Time to untreatable progression by thermal ablation Systemic cancer therapy vacation Quality of life (QLQ C-30)
Cost effectiveness	Hospital stay Re-hospitalisation for complications Room time Ablation time Usage of general anaesthesia Imaging guidance modality

PATIENT TIMELINE AND ASSOCIATED DATA COLLECTION REQUIREMENTS IN CIEMAR



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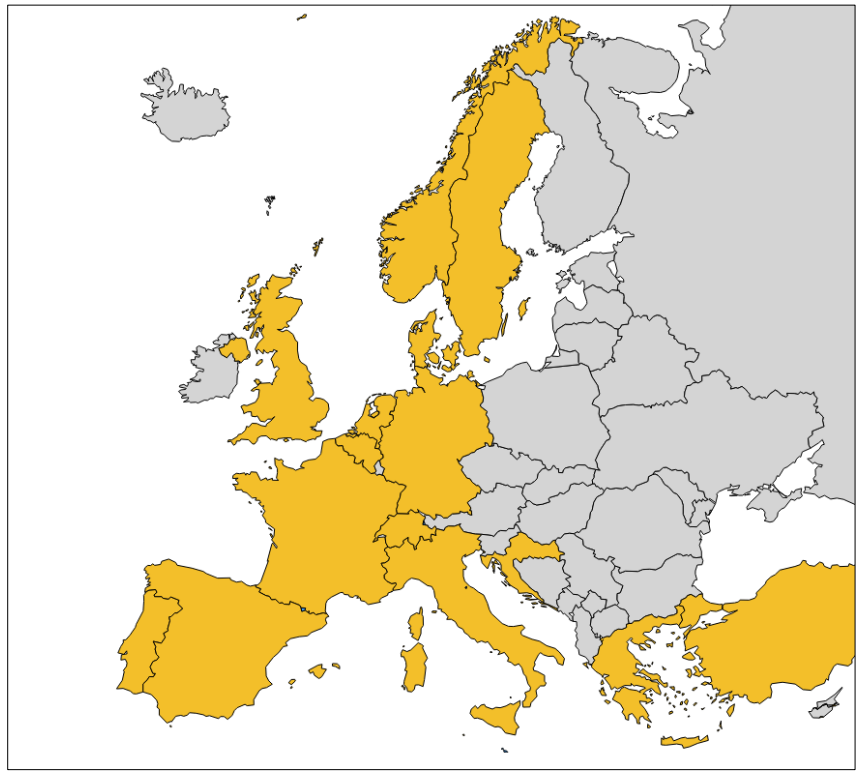
1st wave of hospital invitations

- 72 hospitals
- 15 countries

Country	Nr. of hospitals
Belgium	2
Croatia	1
Denmark	1
France	11
Germany	22
Greece	1
Italy	9
Netherlands	4
Norway	1
Portugal	2
Spain	9
Sweden	1
Switzerland	2
Turkey	1
United Kingdom	6



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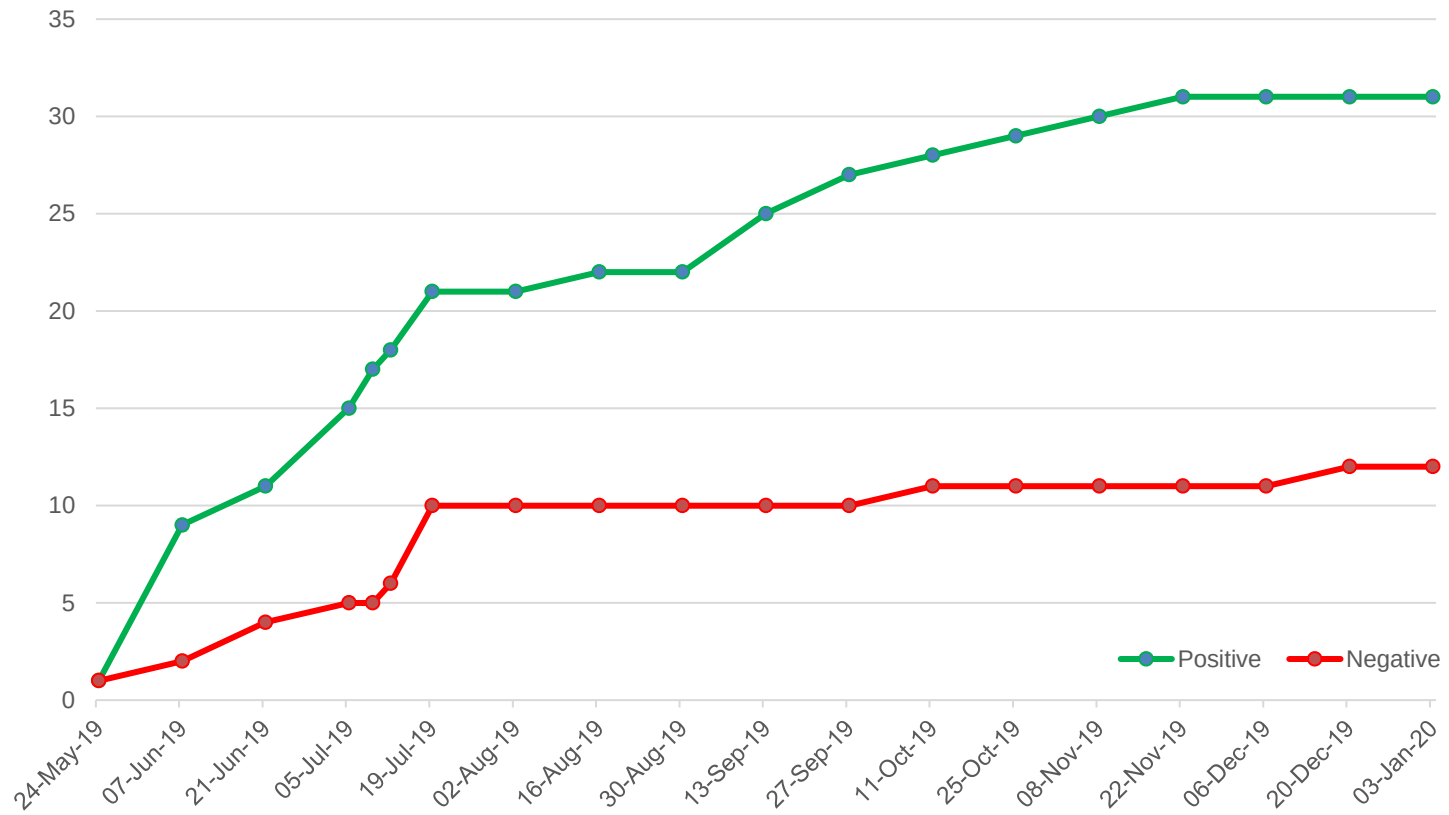
CIEMAR site responses over time (n=72)

Positive responses	Negative responses
32	12



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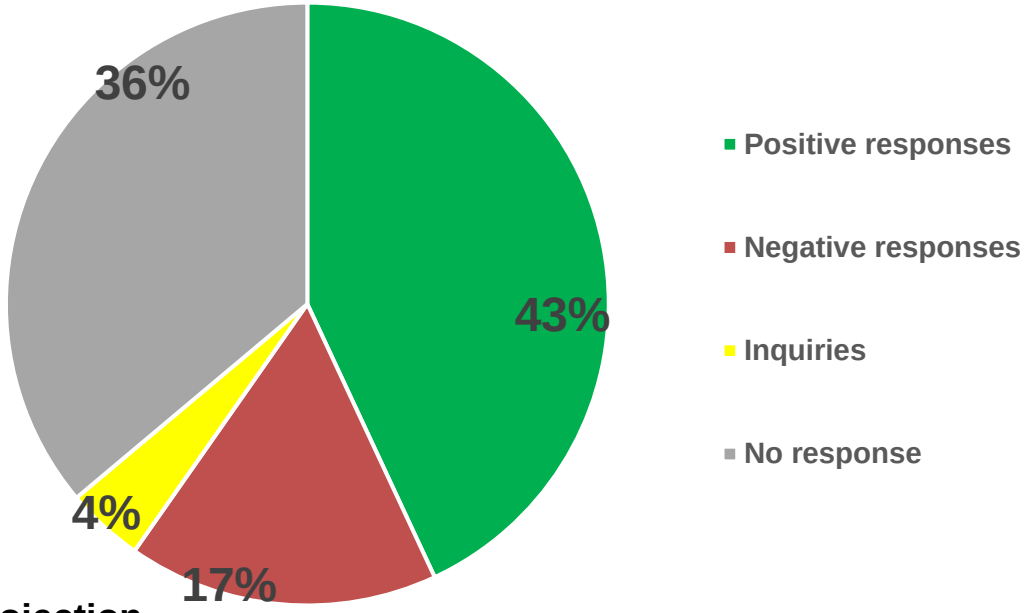
CIEMAR site responses (n=72)

Sent	72
Positive responses	32
Negative responses	12
Inquiries	3
No response	25
Total responses	47
Total response rate	65%



Current response and site enrolment rates still on track for 1000 patient projection.

- **Lessons learned from CIREL:** CIEMAR study site identification was commenced earlier and more thorough. A letter of intent was sent to an extensive list of hospitals compiled with the help of the CIRSE database to gauge initial willingness and ability of sites to participate. The resulting list of hospitals was cross-checked by the Steering Committee and compared with manufacturer information to arrive at a well-targeted list of hospitals to enroll to the study that could realistically provide the required patient numbers for the study.

How did we get there - advocating ablation research

- Discussions regarding a clinical study on thermal ablation for liver tumours – a relatively established therapy for the field – had been conducted in the course of CIRSE Meetings since at least 2013

- Early discussions of a randomised design and multi-device, multi-modality studies were soon frustrated due to difficult negotiations with several competing manufacturers and the shear variety of ablation devices

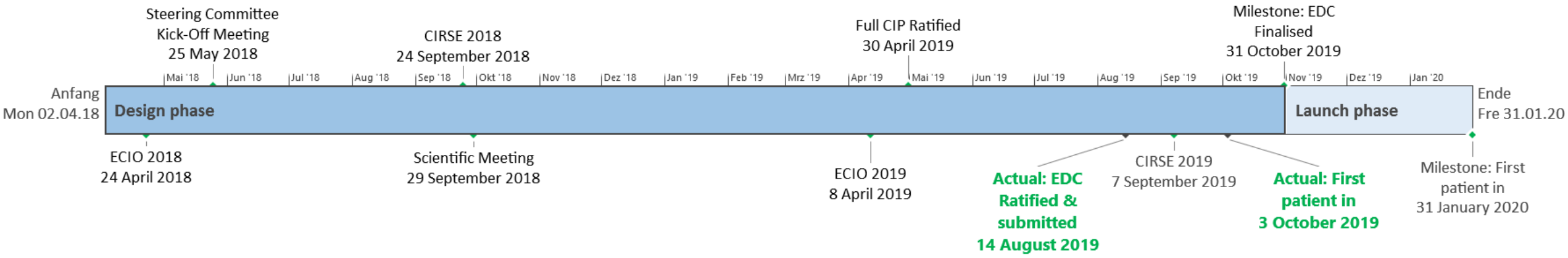
- At CIRSE 2016 the physician group that would later become the CIEMAR Steering Committee met to finalise two key items
  - *Design:* an observational study of substantial size (target 1000 patients) that would provide valuable, actionable information to physicians and be shouldered by CIRSE's infrastructure
  - *Impact:* the group recommended to the Society to accept the trade-off of conducting a well-designed single-device study NOW over years of negotiating/or failing to set-up a larger study

- On February 2, 2017 CIEMAR was submitted to Medtronic's external research programme for funding as an investigator-initiated study with CIRSE as the scientific sponsor

CIEMAR – ahead of schedule

- ✓ Kick-off meeting (25 May 2019)
- ✓ CIEMAR Planning Meeting (29 Sep 2019)
- ✓ Protocol ratified (30 Apr 2019)
- ✓ Electric data capture system finalised (14 Aug 2019, 4 months early)
- ✓ First patient in (3 Oct 2019, 4 months early)

- ✓ 4 sites trained
- ✓ 3 patients included
- 28 H in contracting
- Non-responding site follow-up
- 1st monitoring call



CIEMAR Summary

- CIRSE‘s most mature study in terms of governance, study design, operating procedures, state-of-the-art EDC
- Ambitious target of 1000 patients, study off to a good (early) start
- May provide valuable data from secondary objectives in terms of survival or cost-effectiveness
- Putting the principle of applied observational research into practice and utilising CIRSE’s full capacity
- Has the potential to deepen our understanding of MWA for unresectable CRLM and inform the multidisciplinary decision-making process to maximise patient benefit