Disclosure

Speaker name: Prof. Dr. Ralf – Thorsten Hoffmann, MBA, EBIR

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest
Holmium166 – Do we really need it?

Ralf – Thorsten Hoffmann, MBA
EBIR, FCIRSE, FESGAR
Institut und Poliklinik für Radiologische Diagnostik
Universitätsklinikum Dresden
Situation nowadays

• Multiple studies regarding HCC and mCRC

• Few high quality (?) randomized trials
  – SARAH, SORAMIC, SIRVENIB
  – SIRFLOX, FOXFIRE, FOXFIRE global
RE in BLC C: SARAH Trial

- No difference in overall survival between groups
- RE alternative in Sorafenib-non-responders
- (Partial) PVT no contraindication for RE

Vilgrain V. et al.. Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial. Lancet Oncol. 2017 Dec;18(12):1624-1636
SIRFLOX Studie
Studiendesign

Prospective open-label RCT

**Primary endpoint:** Progression-Free Survival

**Eligible patients**
- Non-resectable liver-only or liver-dominant mCRC
- No prior chemo for advanced disease
- WHO performance status 0–1

**Stratified by**
- Presence of extra-hepatic metastases
- Degree of liver involvement
- Intended use of bevacizumab
- Institution

**Randomized**
1:1
n = 530

```
- n = 263 enrolled
  - mFOLFOX6 (+ bevacizumab) (1)

- n = 267 enrolled
  - mFOLFOX6 (+ bevacizumab) (1)
```

1. Bevacizumab allowed at investigator’s discretion, per institutional practice

**ANZ:** 280 (53%)
**EME:** 191 (36%)
**US:** 59 (11%)

ANZ: Australia, New Zealand; AP: Asia Pacific; EME: Europe & Middle East; US: United States
SIRFLOX, FOXFIRE, FOXFIREGlobal ASCO2017

What are the reasons for these disappointing results?

- Problems with inclusion criteria
- CTx parallel etc.
- Extrahepatic disease
- Dosimetry!
Importance of selecting the *right* patient (HCC)

- Retrospective analysis of the SARAH trial
  - More than 50% of the patients received a suboptimal treatment (<100 Gy tumor dose)

Median OS
6.1 months [95% CI 4.9-6.8]
<100 Gy

14.1 months [95% CI 9.6-18.6]
≥ 100 Gy

Vilgrain et al. ECIO 2018
Patient selection is key to improving treatment outcome (mCRC)

Fig. 5 OS curves estimated by the Kaplan-Meier method according to the treated group (all the lesions received a mean absorbed dose superior to 39 Gy) versus the under-treated group (at least one lesion received a mean absorbed dose inferior to 39 Gy)
Dosimetry might be the game changer
**BSA - Method**

BSA = 0.20247 \times \text{weight} \times \text{height}

\[
\text{TI} = \frac{\text{TV} \times 100}{\text{TV} + \text{LV}}
\]

\[
A_{\text{resin}} = (\text{BSA} - 0.2) + \left(\frac{\text{TI}}{100}\right)
\]

- **BSA** – Body surface area
- **TI** – Tumor involvement
- **TV** – Tumorvolumen
- **LV** – Lebervolumen
BSA - Method

• Simple – dose easy to calculate

• Many studies using the BSA method (incl. SIRFLOX, FOXFIRE, FOXFIRE global)

• Used activity is dominated by height and weight

• Only activity is calculated – but there is no calculation of the dose to tumor / liver
Major drawbacks:
- Small liver – big person
- Risk of overdosing
- Big liver – smaller person
- Risk of underdosing – tumor progression
Partitions model

- Measurement of activity per Partition

- Dose calculation per partition (liver, tumor, lung)

- Calculation of the optimal dose for the tumor – still tolerable for liver tissue and lung

\[ D[\text{Gy}] = \frac{49670 \times A[\text{GBq}]}{m[\text{g}]} \]
Partitionsmodel

\[ TN = \frac{\text{proportionaler Uptake} - \text{Tumor}}{\text{proportionaler Uptake} - \text{Gesunde Leber}} \]

TN: \hspace{2cm} T/N, TBR, TNR, oder auch TLR ger  
Info: \hspace{2cm} aus MAA-scan  
Courtesy U.Graf
Testdosis - TcMAA
TC-99 MAA

• Lungshunting
• Extrahepatic activity
• Liver distribution

Ho-166 microspheres

• Prior to therapy
  – Scoutdose – Ho166
  – CE-mark since 7th January 2019
T/N – Ratio during the pretreatment examinations
Holmium-166 Microspheres testdose vs. therapy

Courtesy M.Smits UMC Utrecht
Imaging capabilities Holmium microspheres
Enabling treatment planning & evaluation

- Personalized local treatment
  - Optimal radiation dose to the tumor
  - Minimal side effects
  - Treatment planning & evaluation (no more black box)
  - Follow-up treatment if needed

Conclusion

- Quirem – Holmium166
  - CE marked since April 2015
  - Studies in the very beginning

Possible advantages:

- Quirem as Scoutdose
- Advantages regarding dosimetry / patients safety

- Dose could be the game changer in further 1st line studies
• Thank you for your attention!
Holmium166 – Do we really need it?

Ralf – Thorsten Hoffmann, MBA 
EBIR, FCIRSE, FESGAR 
Institut und Poliklinik für Radiologische Diagnostik 
Universitätsklinikum Dresden