Holmium166 compared to Yttrium90 radioembolization
Difference & potential advantages

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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
Concept of radioembolization

Selective Application of a high radiation dose into a liver tumor or liver metastases, independently from number, volume and anatomical location within the liver

*however - simultaneously*

(nearly) no radiation within the healthy parenchyma
<table>
<thead>
<tr>
<th></th>
<th>QuiremSpheres®</th>
<th>SIR-Spheres®</th>
<th>TheraSphere®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Matrix</strong></td>
<td>PLLA</td>
<td>Resin</td>
<td>Glass</td>
</tr>
<tr>
<td><strong>Diameter</strong></td>
<td>30 (15-60) µm</td>
<td>32.5 (20-60) µm</td>
<td>25 (20-30) µm</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>1.4 g/cm³</td>
<td>1.6 g/cm³</td>
<td>3.2 g/cm³</td>
</tr>
<tr>
<td><strong>Number of spheres</strong></td>
<td>33 million</td>
<td>33 million</td>
<td>4 million</td>
</tr>
<tr>
<td><strong>Amount per dose</strong></td>
<td>600 mg</td>
<td>914 (1370) mg</td>
<td>110 mg</td>
</tr>
</tbody>
</table>

Quirem Medical B.V.  
Deventer, The Netherlands

SIRTeX Medical Ltd.  
Sydney, New South Wales, Australia

BTG International Ltd.  
London, UK
<table>
<thead>
<tr>
<th>Isotope</th>
<th>Production</th>
<th>Half-life</th>
<th>Decay product</th>
<th>$\beta$-max</th>
<th>$\gamma$-ray</th>
<th>Activity per dose</th>
<th>Imaging</th>
<th>Test dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>QuiremSpheres®</td>
<td>Holmium-166</td>
<td>26.8 hours</td>
<td>Erbium-166</td>
<td>1.77 MeV 48.7%</td>
<td>80.57 keV 6.7%</td>
<td>2-12 GBq</td>
<td>MRI / SPECT</td>
<td>$^{99m}$Tc-MAA -&gt;Ho166</td>
</tr>
<tr>
<td>SIR-Spheres®</td>
<td>Yttrium-90</td>
<td>64.0 hours</td>
<td>Zirconium-90</td>
<td>2.28 MeV 99.9%</td>
<td></td>
<td>2 (of 3) GBq</td>
<td>PET / Bremsstrahlung</td>
<td>$^{99m}$Tc-MAA</td>
</tr>
<tr>
<td>TheraSphere®</td>
<td>Yttrium-90</td>
<td>64.0 hours</td>
<td>Zirconium-90</td>
<td>2.28 MeV 99.9%</td>
<td></td>
<td>5 GBq</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Quirem-Spheres - A new kid on the block – what for?

• Drawbacks of Y90 – products
  – TcMAA as a test substance prior to therapy
  – TcMAA – indirect measurement of potential shunts during therapy (Y90 !!)

  – Glas-, or Resin-Partikel are invisible / not detectable by radiological methods
  – Distribution can be (indirectly) seen via Bremsstrahlen Scan
Treatment planning

Partition model seems ideal (reliable, stable - (even personalized))

Tumordose und liver dose (T/N Ratio)

Not very accurate with $^{99m}$Tc-MAA

differences in particle diameter

differences in specific weight / gravity

potentially other drawbacks (distribution in blood flow ...)

Holmium as a scout dose possibly more accurate

M.Smits UMC Utrecht
• Prior to therapy
  – Scoutdose – Ho166
  – CE-mark planned for 2018
T/N – Ratio in der Behandlungsplanung
Holmium-166 Microsphären als Testdosis gegen Therapieverteilung

Courtesy M.Smits UMC Utrecht
Lung dose using TcMAA – as scout dose – potentially too high

<table>
<thead>
<tr>
<th>Particles</th>
<th>Δ lung dose median</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc-MAA (planar)</td>
<td>5.4 Gy</td>
</tr>
<tr>
<td>$^{99m}$Tc-MAA (SPECT)</td>
<td>2.5 Gy</td>
</tr>
<tr>
<td>$^{166}$Ho scout</td>
<td>0.0 Gy</td>
</tr>
<tr>
<td>$^{166}$Ho therapy</td>
<td>0.0 Gy</td>
</tr>
</tbody>
</table>
• Therapy und Control after therapy
MRI after Holmium application

Primovist® before therapy
Late phase

24 hours after therapy
Q-suite™ enables post treatment dosimetry

- Q-suite™ is a software tool developed by Quirem Medical to convert quantitative SPECT and MR image datasets of QuiremSpheres® into 3D dose distributions.
- The 3D dose distributions may be used for image-based dosimetric verification of dose-to-tumor and dose-to-tissue after the QuiremSpheres® radioembolization procedure.
Primovist MRI with SPECT based isodose lines (manual fusion)

SPECT based absorbed dose
Conclusion

Bremmsstrahlung SPECT

90Y

81 keV

166Ho

Yttrium-based microspheres

Holmium-based microspheres
Conclusion

- Quirem – Holmium166
  - CE marked since April 2015
  - Studies in the very beginning
  - Adopting results (SIRspheres und Theraspheres) – from scientific point of view absolutely incorrect!

- Possible advantages:
  - Quirem as Scoutdose (CE mark missing – 2018)
  - Potentially of advantages regarding dosimetry / patients safety
  - MR imaging – able to detect particles
  - Software for 3D Dosimetry- posttherapeutisch (!)
Future developments
Image-guided Radioembolisation: real-time image-guided Therapie
• Thank you for your attention!
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