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| Name of Sponsor/Company:<br>CIS bio international | |
| Name of Finished Product:<br>ERMM-1 | |
| Name of Active Ingredient:<br>Erbium [$^{169}$Er] citrate | |
| Title of Study:<br>Biological dosimetry in radiation synovectomy of small finger joints with Erbium [$^{169}$Er] citrate | |
| EUDRACT Number:<br>2006-006380-22 | |
| Investigators:<br>Priv.-Doz. Dr. med. Dipl.Phys. Rigobert KLETT (center 01)<br>Dr. med. Ekkehart STELLING (center 02)<br>Michael große DARRELMANN (center 03) | |
| Study Center(s):<br>Center 01: Clinics for Nuclear Medicine, University Giessen, Germany<br>Center 02: Praxis für Nuklearmedizin, Rubensstr. 125, 12157 Berlin, Germany<br>Center 03: Nuklearmedizinische Praxis, Genter Str. 74, 13353 Berlin, Germany | |
| Publication (reference):<br>n.a. | |
| Studied period:<br>date of first enrolment: 8 March 2007<br>date of last completed: 12 December 2007 | Phase of development:<br>IV |
| Objectives:<br>Primary objective of the trial was to assess the radiation exposure after radiation synovectomy (RSO) of phalangeal joints with Erbium [$^{169}$Er] citrate. Radiation exposure was assessed using the technique of biological dosimetry, i.e., the rate of dicentric chromosomes in blood lymphocytes was determined before and after RSO. | |
| Methodology:<br>Prospective, open label, single group (exploratory) clinical trial. Patients served as their own controls (chromosomal aberrations before and after RSO) | |
| Number of patients (planned and analyzed):<br>10 patients planned, 13 patients recruited, 10 patients analyzed | |
| Diagnosis and main criteria for inclusion:<br>Patients with a diagnosis of rheumatoid arthritis or seronegative spondylarthropathy referred to RSO with Erbium [$^{169}$Er] citrate of 1 finger joint (MCP, PIP, DIP) for clinical reasons | |
| Test product, dose and mode of administration, batch number:<br>• Test product: ERMM-1 (Erbium [$^{169}$Er] citrate) as approved for marketing<br>• Mode of administration: 10-40 MBq, intraarticular injection | |

- Batch numbers:
  7010-69, 7012-51, 7032-33, 7035-29, 7036-55, 7039-41, 7032, 7033, 7034, 7039

Reference therapy, dose and mode of administration, batch number:

n.a.

Criteria for evaluation:

**Efficacy:**

Number of dicentric chromosomes before and after RSO

**Safety:**

AEs as elicited upon indirect questioning.

**Statistical methods:**

data listings (exploratory analysis)

SUMMARY - CONCLUSIONS

**EFFICACY RESULTS:**

In the individual patient-based analysis, this study did not show a remarkable difference in dicentric chromosomes after RSO of small joints with Erbium [$^{169}$Er] citrate compared to baseline. In one (1) of ten (10) patients of the per protocol set, a relevant increase in dicentric chromosomes could be detected, whereas in seven (7) of the 10 (10) patients the number of dicentric chromosomes was equal or lower after RSO.

However, when summing up the data of all patients (overall analysis), a slight increase in the total number of dicentric chromosomes and other chromosomal aberrations could be detected.

The chromosomal aberrations observed in this study have been diligently analyzed in a separate expert report by Prof. Dr. Dr. E. Schmid (Title: "Quantifizierung der Strahlenexposition bei der RSO mit dem Radionuklid Erbium-169 am Beispiel von Chromosomenaberrationen in peripheren Lymphozyten", dated January 14, 2008). This expert report is provided as an appendix to this study report. In this expert report, additional statistical analyses (Wilcoxon test) did not provide evidence of a statistically significant increase in the frequency of dicentric chromosomes after RSO with Erbium [$^{169}$Er] citrate. The author concludes that no detectable radiation dose to peripheral blood lymphocytes could be observed with the methods used in this study. An integrated whole body radiation dose could, therefore, not be determined.

**SAFETY RESULTS:**

No AEs had been observed in this study. RSO of small joints using Erbium [$^{169}$Er] citrate is regarded as a safe procedure.

**CONCLUSION:**

RSO with Erbium [$^{169}$Er] citrate is a safe procedure which is not associated with a relevant detectable radiation dose to peripheral blood lymphocytes or a relevant whole body radiation dose.

Date of the report: June 3, 2008