Information brochures for <u>Adults (≥ 18 years)</u>

"Therapy Trial to Determine the Safety and Efficacy of Heavy Ion Radiotherapy in Patients with Osteosarcoma"

Patient:

Dear Mrs/Mr……,

You were diagnosed with a nonresectable osteosarcoma which means that there is no possibility of surgical removal of the tumor without threatening essential organs. Alternatively, you may have refused a possible surgery for personal reasons. In this case, we have to stress that complete surgical removal of the tumor is the method of choice for the treatment of osteosarcoma. Efficacy of *heavy ion radiation therapy* (HIT) has not yet been shown to be as effective as a surgery. Radiotherapy with photons could be an alternative but is also not investigated in systematic trials. To date, other alternatives are not available, without local tumor therapy this disease is not curable.

However, HIT might be suitable to treat the tumor in your bones.

In principle, HIT is a kind of radiotherapy which is very effective for the treatment of nonresectable tumors or tumors with critical localization.

HIT consists of high energetic ionic beams (heavy ions), which deposit a high biological effective dosage with high precision in the tumor bed and with causing only minimal damage to the surrounding normal tissue.

Currently, only a small number of HIT institutions are available worldwide. Currently, the HIT facilities in Heidelberg are the unique place in Europe were patients can be treated with heavy ions. For that reason, there is no long standing experience for HIT in bone tumors.

<u>Objectives of the study:</u>

The aim of this study is an improvement of the long term outcome of patients with nonresectable osteosarcoma and to simultaneously minimize therapy related side effects.

Heavy ions are charged particles which enhance local tumor control in comparison to photon radiation.

Participation to this study may have an advantage for you because HIT can probably

achieve better local control than conventional photon radiation. But there is no guarantee for this advantage.

Realization of HIT:

Before start of Radiotherapy a so called radiation bed respectively a precision mask has to be made. Further MRI and CT-scans are necessary. The whole planning time will be about 1 week.

The whole treatment will last about 6 weeks (5-6 days per week) with a total dosage of 72 CGE. We will start the treatment with protons ((PT) as effective as photons, but with a better dose profile) and than switch to heavy ions for the last approximately 6 radiotherapy sessions.

Every RT session takes approximately 20 minutes.

Position controls of PT/ HIT will be done daily with imaging to reach most optimal precision.

Evaluation of tumor response will be done 2-3 weeks before and 6 weeks after HIT using imaging with MRI, PET and Tc-99 bone scan.

Furthermore, regularly follow-up investigations will be done involving bone scans, MRI, CT, blood tests and clinical examination.

The first **follow-up investigation** will be done **6 weeks after** HIT. Further investigations have to be done **6, 12, 24, 36, 48 and 60 months after** HIT.

In the context of the follow-up acute and late toxicity of HIT will be recorded.

If you agree, we offer to include you in this study.

Risk and side effects:

Side effects (acute and late) of PT and HIT depend on the localization of the tumor and the radiation.

Possible **acute side effects** can be:

- In cases of pelvic tumors: **depression of hematopoesis** with decrease of the red cells, leucocytes or platelets. Sometimes blood or platelet transfusion will be necessary.
- **Mucosa damage**: a) gastrointestinal tract: ulcera, chronic inflammation, colic, diarrhoea, bowel stenosis. b) urinary bladder: inflammation, contracted bladder. In rare cases, surgery has to be done.

- **Skin**: erythema, epitheliolysis, rarely blistering
- In cases of head and neck tumors: **CNS damage** with sickness, vomiting, central nerve palsy, elevated intracranial pressure, headach, dizziness
- **sceletal system**: necrosis, fracture, joint dysfunction, disturbance of growth

Most side effects disappear after the end of HIT.

Possible **long term defects** include:

- **Gastrointestinal tract:** stenosis or perforation with need for surgical intervention, chronic inflammation
- **CNS**: central nerve palsy, cerebral palsy, impaired vision, defective hearing (rare)
- Disturbance of growth
- secondary malignancies
- arteriosclerosis
- Incontinence (rare)
- Impotence (rare)
- Infertility

Long term side effects might be irreversible. In case of radiation induced side effects you must be seen by a radiologist or adequate specialist.

Further information:

The study data will be collected by the principal investigators of the study. Your medical data will be used for evaluation of the study.

Participation in the study is voluntary. You can withdraw from the study at any time without declaration of reasons and without disadvantages in further medical treatment. In case of withdrawal of the study, existing personal data can be destroyed if desired. If you want to change your decision at a later time, please contact the study office. There will be no disadvantages for you concerning further therapy.

Legal requirement concerning confidential medical communication and data protection will be complied with in this study. Only pseudonymized data i.e. without using names will be used for study purposes.