BACKGROUND

- Prognosis of patients with osteoblastic metastases from osteosarcoma is extremely poor.
- Hypothesis for Radium 223 trial in osteosarcoma: 223Ra can be safely administered to pts with osteosarcoma and early response and/or resistance signals can be assessed by correlative imaging studies and biomarkers.
- Bone forming osteosarcoma metastases are common in extra-osseous sites especially when metastatic in the lungs.
- Since bone forming tumors do not shrink in response to therapy, intra-tumoral and inter-tumoral changes are challenging to evaluate using conventional imaging modalities.

METHODS

- Investigator initiated, single institution, phase I, dose-escalation trial of 223Ra in recurrent or metastatic osteosarcoma.
- To be eligible the patient must have recurrent osteosarcoma with indicator lesion that has uptake of 99mTc-MDP on bone scan or NaF PET scan.
- A dose-escalation trial of 223RaCl (50, 75, and 100 kBq 223RaCl, /kg) enrolled pts age 15+ w advanced osteosarcoma (Fig.1).
- Molecular imaging with technetium (Tc)-99m bone scan, FDG PET or sodium fluoride-18 (NaF) PET was done at baseline and at restaging.
- We developed a PET radiomics method for analyzing NaF, i.e. radioactive 18F -atom concentration in soft-tissues, approximately 1000 concentration data points for 18F per 1 cm² metastatic tumor.
- We analyzed data from the SUV intensity values, we obtained (i) the histogram of intensities, (ii) entropy value. The fractions of voxels were plotted against intensity bins.

SCHEMA

- Bone scan 99mTc-MDP avid osteosarcoma or NaF PET CT
  - (indicator lesion= local recurrence or metastasis)
- Alkaline Phosphatase, Bone turnover markers and Base line Imaging
- Alkaline Phosphatase, Bone turnover markers and Post dose #3 Imaging

Figure 1: Schema of trial

 imaging: Three modalities will be compared pre vs after dose 3 and after dose 6

ΔSUV of 18F PET

ΔSUV NaF PET CT

Δ activity 99mTc-MDP SPECT-CT

Figure 2: Ra223 releases 5 alpha and 3 beta particles

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RESULTS

- We applied this method to two lung metastases (Fig.2) and two soft-tissue metastases (one example in Fig. 3), before and after two cycles of Ra-223-treatment.
- The metastatic tumors were 80-120 cm² in size. This alpha-therapy is effective only in the close vicinity of the target cell, i.e. 4-5 cell diameter range.
- All these metastases demonstrated mixed type of response, where RECIST or PERCIST type of criteria do not apply.
- In these metastatic sites there were abundant conformational changes which could be considered as therapeutic changes.
- These can be explained e.g. by changes in entropy, kurtosis. The configuration, amount of distortion etc. can give us guidance of responding tumor parts.

CONCLUSIONS

- Radiomics can inform intra-tumoral and inter-tumoral heterogeneity in response of bone forming osteosarcoma to alpha particle therapy.
- With the help of this new PET radiomics method for 18F -atom concentration, this can be studied in detail, bone formation regions can be identified.
- Characteristic changes in entropy may be used to quantify the treatment response. Further larger validated studies are warranted.