SARC bone tumor studies

- Imatinib – single-arm, multi-cohort, phase II
- Gem/Tax – single-arm, 3 cohort, phase II
- Dasatinib – single-arm, multi-cohort, phase II
- R1507 – single-arm, multi-cohort, phase II
- AZD5030 – randomized, placebo-controlled, adjuvant

SARC001: Imatinib in unresectable or metastatic sarcoma

- Primary endpoint:
  - **4-month PFS rate** in unresectable or metastatic sarcoma failing one or more prior treatment regimens
- Bayesian design
  - Target >30% 4-month PFS
- Overall study accrual
  - N= 241 patients
- Osteosarcoma accrual
  - N= 27 patients
  - 6 sites
  - 3.5 years
- Conclusion: did not meet level of activity

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SARC003: Gemcitabine/Docetaxel in metastatic bone tumors

- Primary endpoint
  - **Objective response rate** in recurrent Osteosarcoma or Ewing's sarcoma and Chondrosarcoma
- 3 cohorts - analyzed separately
  - >35% RR for osteosarcoma and Ewing's
  - >20% RR for chondrosarcoma
- Osteosarcoma accrual
  - N=14
  - 1 year
  - 8 sites
  - Arm closed for futility

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SARC009: Dasatinib in selected subtypes of metastatic sarcoma

- Primary endpoint
  - Response rate + 6-month progression-free survival
- Bayesian hierarchical design
  - Target >25% rate
- Overall study accrual
  - N= 344
  - Activated 5/07
  - 18 sites
- Osteosarcoma accrual
  - N= 47
  - 2 years (paused several times for analysis)
  - 17 sites

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SARC011: IGF-1R antibody in Ewing's, Osteosarcoma, Synovial, Rhabdomyosarcoma and other sarcomas

- Primary endpoint
  - Objective response rate
- 2-stage design, separate cohort
  - Target >30% ORR
- Overall study accrual
  - N= 305
  - 21 months
  - 39 sites (EU/Australia-18 sites, US-21)
- Osteosarcoma accrual
  - N= 38 (EU/Australia-6, US 32)
  - 8 months
  - 14 sites (EU/Australia-2, US-12)

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SARC012: SRC-kinase inhibitor in metastatic osteosaroma (lung only) following complete resection

- Primary endpoint
  - 2-year progression-free survival rate
- Target – 60% relative improvement (53% vs 33%)
- Study accrual
  - N= 5
  - Open to accrual for 11 months
  - 12 sites
    - 5 patients accrued from 3 sites

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SARC experience

- Rapid protocol development and implementation
- Rapid accrual to phase II trials
- Bayesian design requires “real-time” data entry and analysis
- Large pool of adults with osteosarcoma