

## Data Supplement 2: Results

### Case vignettes

One patient who achieved a CR was aged 13 years with metastatic alveolar rhabdomyosarcoma (RMS) at diagnosis who had received two prior lines of therapy including vincristine and irinotecan (VI). The patient received 12 cycles of VI (in a phase II Innovative Therapies for Children with Cancer [ITCC] trial of VI ± temozolomide) for first relapse between January 2017 and December 2017 as systemic therapy in addition to surgical resection and adjuvant radiotherapy. Disease recurrence occurred in February 2019 and the patient was included in the present study in March 2019. This patient had a 2.4 cm target lesion and a non-target lesion in the iliac region, which were no longer present at first post-baseline tumor assessment during treatment with regorafenib 82 mg/m<sup>2</sup> (sequential). Another patient aged 4 years with metastatic alveolar RMS who received first-line treatment in the BERNIE study (6 months of induction chemotherapy including ifosfamide, vincristine, actinomycin D and doxorubicin followed by 12 cycles of maintenance with low-dose cyclophosphamide + vinorelbine and radiotherapy) (1), had local relapse in the leg and was treated with complete resection and six cycles of VI; further mediastinal relapses were treated by surgery, radiotherapy, and chemotherapy (topotecan/carboplatin, topotecan/cyclophosphamide, and carboplatin/etoposide). Molecular tumor profiling (next generation panel sequencing) revealed that the patient's tumor was *P53* wild type. The patient was included in the present study aged 11 years following a fourth disseminated relapse; progressive reduction in tumor lesion size was seen (**Supplementary Fig. S2**), and the patient received prophylactic focal irradiation when the last remaining lesion (popliteal

fossa) was cleared; this patient remained in sustained complete remission after 34 cycles at the last follow up.

## References

1. Chisholm JC, Merks JHM, Casanova M, Bisogno G, Orbach D, Gentet J-C, et al. Open-label, multicentre, randomised, phase II study of the EpSSG and the ITCC evaluating the addition of bevacizumab to chemotherapy in childhood and adolescent patients with metastatic soft tissue sarcoma (the BERNIE study). *Eur J Cancer* **2017**;83:177-184.