Alveolar Soft Part Sarcomas: a Tertiary Care Indian Centre Experience : the therapeutic journey from nihilism to cautious optimism

Jyoti Bajpai*, Simha V, Bhargav P, Srinivas S, Rekhi B, Banavali SD.

Tata Memorial Hospital And Advanced Centre for Treatment, Research and Education In Cancer (ACTREC), Homi Bhabha National Institute (HBNI), Parel, Mumbai, Maharashtra, India

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Introduction

- Alveolar soft part sarcoma (ASPS) is an ultra-rare and chemo refractory sarcoma.
- The natural history of ASPS is unique with an extremely indolent behavior with late symptomatic metastasis.
- Despite being a chemo resistant disease, it is known for prolonged survival even in a few metastatic patients with spontaneous disease stabilization and indolent disease behavior.
- Targeted therapy with antiangiogenic agents inclusuive of tyrosine kinase inhibitors(TKI) and Immunotherapy has shown promise
- However, tyrosine kinase inhibitors feasibility data is sparse from low-middle income countries and merits exploration.

Methods

- This is a retrospective audit of ASPS patients treated at TMC from Jan 2002 to August 2021 .
- Patients with confirmed histopathological diagnoses of ASPS were included in this analysis.
- Clinical, demographic, and treatment-related data were collected from Casefiles and Electronic medical records.
- Demographic data [Age, Gender]
- Clinical data [Tumor site/Size/Stage/Metastatic or Localised] and
- Treatment [Surgery/Radiotherapy/Chemotherapy/ Antiangiogenic targeted therapy] were analyzed.
- The choice of systemic therapy was Ifosfamide (5.4-6g/m2)-adriamycin (60-75mg/m2) combination in the initial 14 years from 2002-2016; but over the next three years, with the evolution of literature, the treatment choice was anti-angiogenic therapy with tyrosine kinase inhibitors sunitinib, sorafenib and pazopanib.

Methods

- We compare and contrast the patterns of care in the systemic therapy of ASPS with advanced disease with multi-tyrosine kinase inhibitors vs. conventional chemotherapy vs best supportive care and compared their respective outcomes

Results

- There were 85 patients with a median age of 32 years; 48 (57 %) were males.
- Commonest primary site was extremities in 57(67%), 31 (37%) were de-novo metastatic(mASPS).
- Among the 54 (63%) non-metastatic patients, 24 relapsed and became metastatic and hence 55(65%) patients were treated for their metastatic disease at some point.

ASPS :Non-metastatic Cohort

- Among the 54 nm-ASPS, 41(76%) underwent surgery, 34 (63%) received adjuvant and 4 received definitive radiation, 2 received adjuvant chemotherapy.
- At a median follow up of 27(95% CI-9-46) months, median EFS was 46(95% CI 0--142) months and predicted 3& 5-year EFS were 54%& 47% respectively.

Metastatic-ASPS

- Of the 55 total patients , 23 (41%) received best supportive care (BSC).
- Ten(18 %) received TKI (7-pazopanib, 3-sunitinib) and remaining received other systemic therapies.
- Eight (80%) had clinico-radiological responses, including 5(50%)-partial responses and 3(30%) stable disease.

ASPS: Metastatic Cohort: Outcomes

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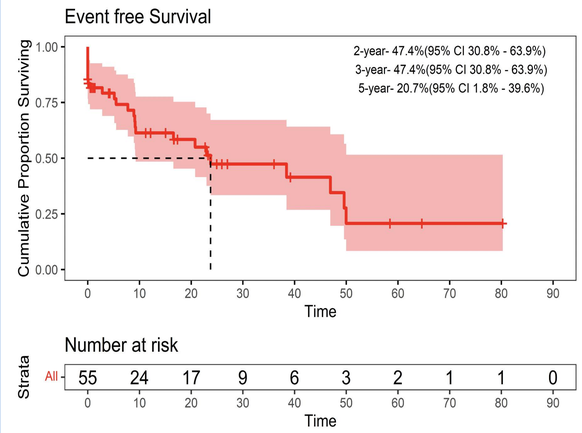
Metastatic-ASPS: Outcomes



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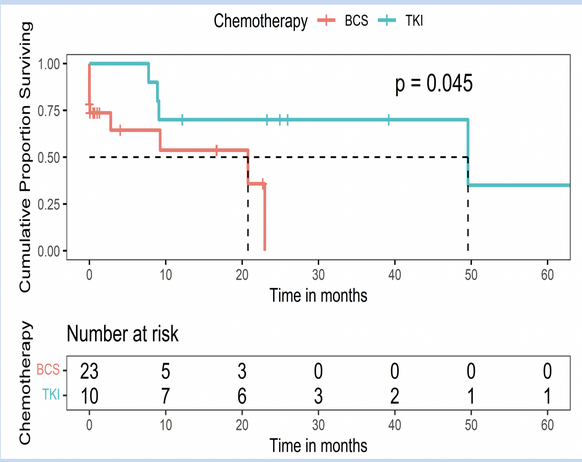

TOLERANCE

- The TKI were well tolerated with significant grade 3/4 toxicities seen (with 800 mg dose) in 3 patients including diarrhea (3), mucositis (1), hyponatremia (1).
- De-escalation to 600 mg leads to good tolerance in 7(70%).
- Majority were given 600 mg dose.

Discussion

- ASPS is a systemic disease with high metastatic potential and poor chemo-sensitivity.
- The large series in ASPS suggest comparable practice pattern and results to published literature in nmASPS.
- Our institute practice has evolved from a policy of therapeutic nihilism to cautious optimism with antiangiogenic therapy leading to meaningful responses.
- With many novel agents in the pipeline and pathway-driven Basket trials and collaborative prospective clinical trials, the future of management of ASPS looks promising

Conclusions

- There was a transition in treatment approach for mASPS from the best supportive care towards Tyrosine Kinase inhibitors with good clinical benefit and acceptable tolerance.
- Tyrosine Kinase inhibitors are a feasible standard of care option to mASPS even in low-middle income countries.

*drjyotibajpai25@gmail.com
@JyotiBajpai01