CORRESPONDENCE

Refractory ALK-Positive Anaplastic Large Cell Lymphoma: Long Term Survival with Crizotinib

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Received: 1 September 2017 / Accepted: 6 October 2017 / Published online: 4 November 2017
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Keywords Anaplastic large cell lymphoma ALK+ve · Crizotinib · ALK · Targeted therapy

Dear Editor,

Anaplastic large cell lymphoma, ALK positive is characterized by increased expression of the ALK protein. Though two-thirds can be cured with chemotherapy, patients with refractory disease have limited options [1]. ALK has been successfully targeted by crizotinib in lung cancer and reports show success in ALK+ lymphomas also [2].

A 38-year female presented with right iliac fossa pain in June 2014. She had a large soft tissue mass in the right ilio-psoas region extending from the level of L1 to L5 vertebra with bony destruction of L3 vertebra (Fig. 1a, b). Biopsy from the mass showed ALK+ ALCL. She started CHOP chemotherapy but progressed after cycle 1. With a more intensive therapy (LMB-89, group B protocol), she initially responded, but again

progressed after cycle 5. The lymphoma continued to progress on salvage DHAP chemotherapy. She developed intense pain in the iliolumbar region which was poorly controlled with morphine and resulted in spasm of the iliopsoas muscles and fixed flexion at right hip. She received radiation with partial relief of pain but remained bed bound in poor general condition. At this point, we started oral therapy with crizotinib 250 mg twice daily. Within 2 weeks, there was complete resolution of pain and patient was able to walk. Follow up CT scans showed progressive improvement and PET-CT scan done after 6 months of crizotinib showed complete metabolic response (Fig. 1c, d). Patient was unwilling for stem cell transplant and hence crizotinib was continued. She has completed 30 months of crizotinib till now and remains in complete anatomic and metabolic response.

This report highlights a patient with chemo-refractory ALK+ ALCL showing a dramatic and sustained response to ALK-targeted therapy. Complete response to crizotinib is not uncommon in ALK+ ALCL [2, 3].

The fusion protein NPM-ALK promotes tumorigenicity by binding to and constitutively activating a host of cellular signalling proteins, including those in the signalling pathways of signal transducer and activator of transcription 3 (STAT3), *MEK/ERK*, mammalian target of rapamycin (mTOR) and phosphoinositide 3 kinase (PI3K)/Akt leading to cell proliferation and resistance to apoptosis. Crizotinib exerts its therapeutic effect by inhibiting the phosphorylation of the ALK tyrosine kinase and thus blocks the downstream effects of this oncogene [4]. The duration of therapy is currently unclear and the longest duration of reported in literature is 37 months [5]. Though crizotinib may be considered as a reasonable option in patients with chemo refractory

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Fig. 1 Pre-treatment PET-CT showing the metabolic activity and the extent of the soft tissue mass from the level of L1 to L5 vertebrae on right side (a) with evidence of bony involvement (b). After therapy

with crizotinib there was complete metabolic response with small fibrosed soft tissue irregularity in the right lower paravertebral region (c, d)

ALK+ ALCL, this particular case represents an exceptional response. Further studies are needed to establish more long term data regarding efficacy and safety.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This is a retrospective data analysis and no patient identifying information is being included in the manuscript. As per our Institution policy, we don't require ethical approval for retrospective analysis.

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