Dear Dr. Lin,

My name is Yoram Shahar, and Jeff Sturm gave me your email. He spoke highly of you and suggested contacting you for advice regarding my wife’s particular case:

My wife, Yael, has Alk-positive NSCLC. We live in Tel Aviv, Israel.

Yael’s ALK pathology results show PMS2 Q567\* mutations and a TMB of 10 mutations/Mb. We would appreciate your professional opinion about using immunotherapy for this MMR NSCLC with a relatively high mutational burden for Alk.

Here are some other relevant data you may need to consider:

A 10-mm diameter tumor was excised by segmentectomy in June 2017. The pathology of that specimen showed an Alk rearrangement of exon 20, and Dnmt3a s770w.

In November 2019, a cancer recurrence was evident in a right supraclavicular node (1.2 cm) and in mediastinal (retrocaval) nodules (up to 1.7 cm in size). My wife initiated a Xalcori regimen, but had to stop it after 3 weeks due to pneumonitis. Instead, she underwent 66 Grey radiation and was treated with 6 rounds of carbo-Pemetrexed without TKIs.

In January 2021, a recurrence was apparent in the mediastinum (station 7, right hilum). Pathological examination of the lesion showed an ALK rearrangement of exon 20 PMS2 Q567\* with a TMB of 10 mutations/Mb (MSI stable).

She was started on Brigatinib and has had no evidence of disease in a PET scan for 18 months.

We have consulted a few oncologists in Israel. Two of them believe that, in the event of a future recurrence, my wife should be prescribed immunotherapy in addition to the present TKI or as a next step.

However, we would like your expert opinion on whether to use immunotherapy and if so, which specific agent to use. Should the regimen include the TKI, and should it be concomitant with it or sequential? Should my wife be offered immunotherapy before disease progression? Please do not hesitate to contact us with any questions. We are happy to provide any additional information you might require to assess our case.

We appreciate your time and hope you will be able to help us. Thank you very much for your thoughts.

Sincerely,

Yael and Yoram Shahar

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