**Professor Nir Peled**

March 19, 2020

1. Has been taking Brigatinib for approximately one month which is well-tolerated.
2. Has completed radiation – in d2 with the return of sensation in the hand.
3. Guardant test EML4ALK only.
4. Also performed FoundationOne Liquid – ALK EML4 variant 2. In VUS-BRCA2, CDK12, STK11.
5. Chest CT dated March 17, 2020 is stable, including the pulmonary parenchymal and lymphangitic findings and there are no significant dynamics in comparison with the previous exam.
6. Presently, consultation on the phone with her son and Ayala. Clinically stable. Is continuing Eliquis 2.5 mg twice a day.
7. In summary, respiratory stability. Lack of clear resistance mechanism in the Liquid test. We will continue without change while performing follow-up with CT of the chest, PET-CT in another month while taking Brigatinib 180 mg once a day and Eliquis without change.

March 29. 2020

1. Increasing respiratory exacerbation in the last few weeks, to a level of 87% saturation without oxygen.
2. Performance of CT-guided biopsy, for characterization of the disease. A CT-guided puncture was performed on the left side, some neoplastic matter which is doubtful to be sufficient for extensive molecular investigations. Some of the analyses will be performed at Rambam Hospital.
3. Observation of the CT biopsy, impression of extensive symmetric pneumonitis, may be secondary to Brigatinib. Alternatively, may be exacerbation of lymphangitic dissemination. However, at the beginning of the disease, the lungs looked better.
4. Started Carbo, Alimta today, reports remarkable respiratory improvement under steroids as preparation for chemotherapy to bear the pulmonary pneumonitis which may be attributed to Brigatinib.

Therefore, I support:

1. Continue Carbo + Alimta once every three weeks for three courses
2. Continue Eliquis 2.5 mg twice a day
3. Calcium supplement due to involvement of bone disease. Wait with XGEVA at this stage
4. Start prednisone (instead of dexamethasone) at a dosage of 40 mg a day for a period of one week and then 30 mg a day for a period of three days and then 20 mg a day for a period of three days, and then 10 mg a day for a period of one week, and then 5 mg a day for a period of two weeks.
5. Avoid Brigatinib due to suspected pneumonitis. Update the answers with the biopsy.
6. Follow-up with CT of the chest without contrast agent and after three treatment courses, MRI of the brain.

May 07, 2020

1. After two courses of Carbo + Alimta. After treatment difficulty and lying down for a week with loss of appetite and low mood.
2. Reduced prednisone gradually, around the first treatment. Around the second treatment, took only dexamethasone before the treatment. After treatment, did not take steroids and had a lot of fatigue and nausea.
3. PET-CT dated May 5, 2020 with significant improvement in the pulmonary parenchyma with the disappearance of most of the lymphangitis. A number of sclerotic lesions and uptake within (D11, D12, D5), there is mild back pain.
4. Reports general improvement in sensation including walking 5 km, whereas before chemotherapy required oxygen regularly.
5. Molecular investigation at Rambam Hospital with ALK positive and without additional findings.
6. MRI of brain from April 26, 2020 without metastases.
7. Therefore, good response to chemotherapy, clinically and imaging. The osseous findings are with uptake within the sclerotic lesion and therefore, maybe associated with the interval between the two PET CT exams and not necessarily indicate progression under chemotherapy.

PS test=0. Auscultation very good, bilateral. Peristalsis normal.

Therefore, recommend:

1. Continue Carbo Alimta for another two courses
2. PET-CT after two courses
3. To answer the family’s question – I do not see a need to add an ALK inhibitor
4. Please report any event of exacerbation of back pain. Continue XGEVA once every two months.