ESMO PRECEPTORSHIP PROGRAMME

MARIJA KARAKOLEVSKA ILOVA

Oncologist radiotherapist

1. University of Goce Delcev, Stip
2. Clinical Hospital Stip

RNMacedonia

DISCLOSURE OF INTEREST

- NONE

Hereditary cancer syndromes, such as Li-Fraumeni syndrome (LFS), arise from germline pathogenic variants in the TP53 gene.

The TP53 gene is an essential tumor suppressor that identifies DNA damage and controls gene expression to preserve genomic stability.

LFS is characterized by a markedly increased predisposition to early-onset malignancies, including breast cancer, primary central nervous system (CNS) tumors, and soft tissue and bone sarcomas.

Among the reported variants associated with LFS is the c.451C>T mutation / p.Pro151Ser, which follows an autosomal dominant pattern of inheritance and can be transmitted from affected parents to their offspring.

The c.451C>T mutation is a high-frequency pathogenic variant classified as a “hotspot” mutation, as it occurs in more than half of human cancer types.

This variant is located within the DNA-binding domain of TP53 and results in a loss of function, thereby contributing to cancer progression.

Another variant at the same position, c.451C>A mutation / p.Pro151Thr, is also recognized as pathogenic and is well documented in Li – Fraumeni syndrome.

CASE PRESENTATION

The case involves a 57-year-old female patient referred for genetic counseling.

(**2018/ 50 years old**)

Hihg grade endometrial stromal sarcoma. St post HTA cum BSO.
FIGO T1b pNx pMx pLO pVO St IB (2018). St post chemotherapy

6 MONTHS AFTER

(**2019**)

GIST abdominis.St. post operationem. Stg II.

NO GENETIC COUNSELING !

(**2024/ 54 years old)**

Ca ductale mammae lat sin. Ms lgll lat sin. Status post FNAB
cTNM= cT3 cN2 M1
IHC= ER neg, PR neg, Her2/neu 3+, Ki67= 50-55%
CT scan: Ms pulmonum bill. Effusio pleurae lat sin.

→

GENETIC COUNSELING !!!!!

1. First line chemotherapy: Doc75x6 (16/04/2024-06/08/2024)
2. First line target therapy: Pertuzumab (16/04/2024- 06/08/2024)

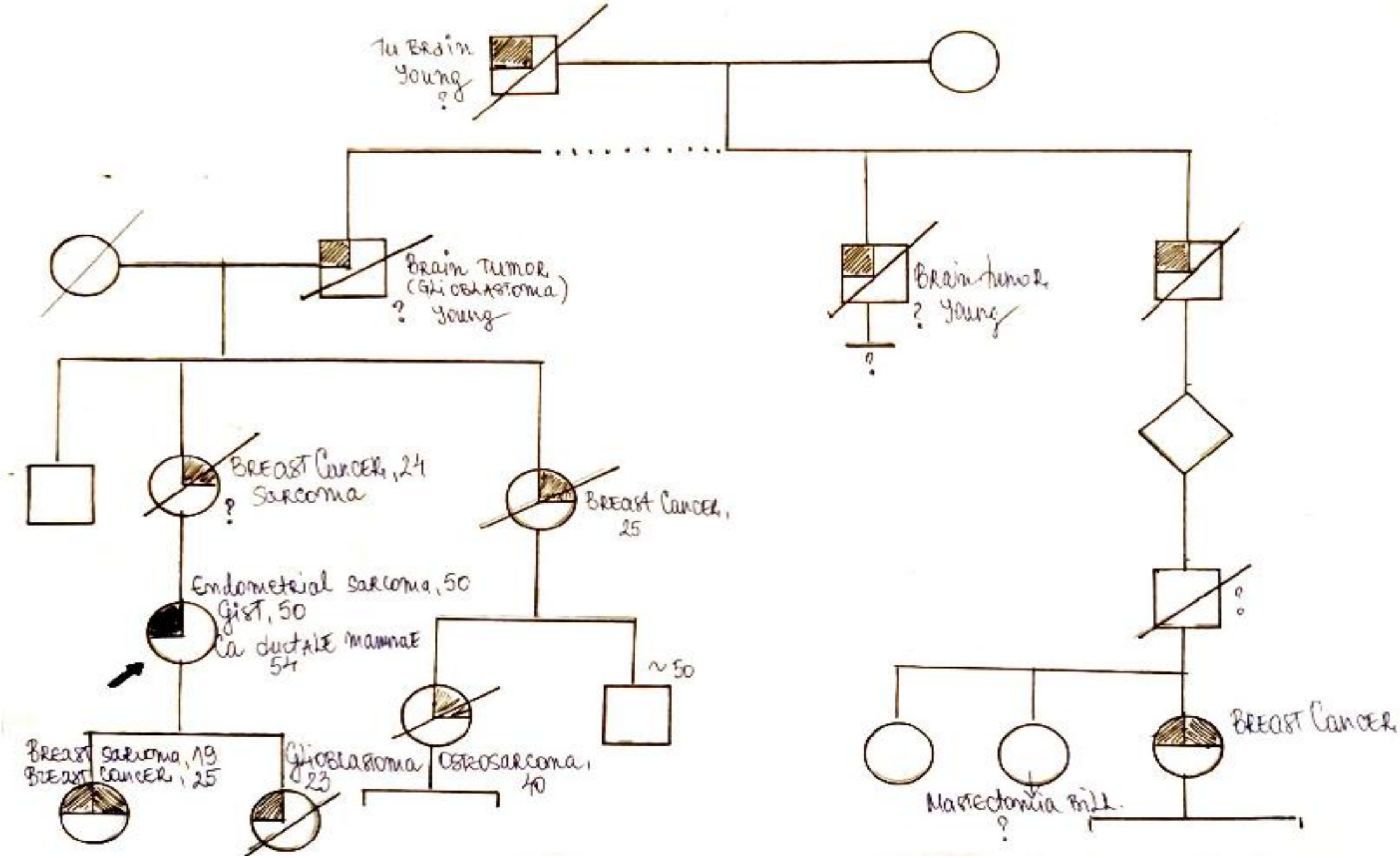
CT scan: (13/8/2024) Ms pulmonum, Ms hepatis, Effusio pleurae l.sin, Ms lgll mediastini, paraaort, paracavales, Ca mammae, ms lgll axillae, supra et infraclav. l.sin / ***desease progresion***

3. Second line target therapy: Ado-trastuzumab emtasine (30/08/2024- 11/2025)

The patient has two daughters.

One daughter was diagnosed with glioblastoma at 24 years of age, while the other daughter developed a breast sarcoma at 19 and a contralateral ductal carcinoma at 23.

Interestingly, the patient is adopted, and information regarding her biological mother was obtained heteroanamnestically from the patient herself.


Tu Brain
young
?
Brain Tumor
(Glioblastoma)
? young
Brain tumor
? young
?
Breast Cancer, 24
Sarcoma
?
Breast Cancer,
25
Endometrial Sarcoma, 50
Gist, 50
Ca ductale mammae
54
~50
Breast Sarcoma, 19
Breast Cancer, 25
Glioblastoma
23
Osteosarcoma,
40
?
Breast Cancer
Mastectomia bill.
?

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ESMO Education Department
c/o **European Society for Medical Oncology (ESMO)**
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
courses@esmo.org