



การแพทย์จีโนมิกส์สู่การวินิจฉัยและการรักษาที่แม่นยำ

นายแพทย์ภาสกร วันชัยจิระบุญ พ.บ. วทม.

อายุรแพทย์มะเร็งวิทยา และ อายุรเวชพันธุศาสตร์

กรรมการและ ผู้ช่วยเลขานุการแพทยสภา (2561-ปัจจุบัน)

เลขาฯ อนุกรรมการ เวชศาสตร์จีโนมแพทยสภา (2563 - ปัจจุบัน)

เลขาฯ คณะทำงานจัดทำหลักสูตรการให้คำปรึกษาแนะนำทางพันธุกรรม ภาควิชาชีวเวชศาสตร์ (2563 - ปัจจุบัน)

กรรมการและ รองเลขานุการ ราชวิทยาลัยอายุรแพทย์แห่งประเทศไทย (2563-ปัจจุบัน)

ผู้ช่วยผู้อำนวยการ รพ.พระปกเกล้าดูแล ศูนย์เชี่ยวชาญระดับสูงด้านมะเร็ง และ Health technology จันทบุรี (2562 - ปัจจุบัน)

ประธานคณะทำงานศูนย์จีโนม และวิจัยทางคลินิก รพ.พระปกเกล้า จันทบุรี (2563- ปัจจุบัน)



Est 17th April 2019

- 10 Storey Buildings
190 Beds
- Service
 - Surgical oncology
 - Medical Oncology
 - Radiotherapy
 - Interventional Oncology
 - Nuclear Medicine
 - Diagnostic Oncology
 - Palliative Oncology
 - Research Center

Surveillance/Screening Test

Start	Test	Interval	Stop
≥ 40 Y	Mammogram	1 Y	As long as healthy
average risk ≥ 45 Y	FOBT Sigmoidoscopy Colonoscopy	1 Y 5 Y 10 Y	As long as healthy
High risk 55-74 Y	Low dose CT	1 Y x 3	> 74 Y
≥ 21 Y or 3 Y หลังจากเริ่มมีเพศสัมพันธ์ ครั้งแรก	PV + PAP HPV DNA	3 Y 5 Y	> 65 Y
≥ 50 Y with life expectancy ≥ 10 Y	PSA	1 Y	As long as healthy
High risk	AFP + U/S liver	6 m	No data



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ข้อบ่งชี้ของการตรวจหา Germline Test (เลือกอย่างน้อยหนึ่งข้อดังนี้)

- ☐ ผู้ป่วยมีประวัติเป็นมะเร็งเต้านมเมื่ออายุไม่เกิน 45 ปี โดยอายุเมื่อวินิจฉัยคือ ปี
- ☐ ผู้ป่วยมีประวัติเป็นมะเร็งเต้านมเมื่ออายุไม่เกิน 50 ปี และมีข้อใดข้อหนึ่งดังนี้
 - ☐ มีประวัติเป็นมะเร็งเต้านมซ้ำ (second primary)
 - ☐ มี first degree relative เป็นมะเร็งเต้านม
 - ☐ มี first หรือ second degree relative เป็นมะเร็งตับอ่อน
- ☐ ผู้ป่วยเป็นมะเร็งเต้านมชนิด triple negative เมื่ออายุไม่เกิน 60 ปี
- ☐ ผู้ป่วยเป็นมะเร็งเต้านมเมื่ออายุใดก็ได้ และมีข้อใดข้อหนึ่งดังนี้
 - ☐ มี first degree relative เป็นมะเร็งเต้านม, ตับอ่อน, ต่อมลูกหมาก อย่างน้อย 2 คน
 - ☐ มี first degree relative อย่างน้อย 1 คนเป็นมะเร็งเต้านมอายุน้อยกว่า 50 ปี
- ☐ ผู้ป่วยเป็นมะเร็งเต้านมเพศชาย / มะเร็งต่อมลูกหมากชนิดแพร่กระจาย
- ☐ ผู้ป่วยมีประวัติเป็นมะเร็งเต้านม และมีข้อใดข้อหนึ่งดังนี้
 - ☐ มีประวัติเป็นมะเร็งชนิด sarcoma ร่วมด้วย
 - ☐ มีประวัติเป็นมะเร็งชนิดอื่นเมื่ออายุ 45 ปีหรือน้อยกว่า
 - ☐ มีประวัติเป็นมะเร็งชนิด adrenocortical cancer, glioma, choroid plexus cancer
 - ☐ มี first หรือ second degree relative อย่างน้อย 1 คนเป็นมะเร็งชนิด sarcoma
 - ☐ มี first/second degree relative อย่างน้อย 1 คนเป็นมะเร็งเมื่ออายุ 45 ปีหรือน้อยกว่า

☐ ผู้ป่วยมีประวัติเป็นมะเร็งรังไข่ / ตับอ่อน

☐ ผู้ป่วยมี adenomatous polyps >10 อันหรือ hamatoma >2 อันในลำไส้

☐ ผู้ป่วยเป็นมะเร็งลำไส้ใหญ่ / เยื่อบุผนังลำไส้ และมีข้อใดข้อหนึ่งดังนี้

☐ มีอายุเมื่อแรกวินิจฉัย < 50 ปี

☐ มีประวัติมะเร็งลำไส้ใหญ่ (synchronous/metachronous) / เยื่อบุผนังลำไส้มาก่อน

☐ มี first degree relative อย่างน้อย 1 คนเป็นมะเร็งลำไส้/เยื่อบุผนังลำไส้ อายุ < 50 ปี

☐ ตรวจพบความผิดปกติของ MMR protein หรือมี MSI-H ในชิ้นเนื้อมะเร็ง

☐ ผู้ป่วยเป็นมะเร็งตั้งแต่ 2 ชนิดขึ้นไปหรือมีลักษณะของ hereditary cancer syndrome คือ

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☐ ผู้ป่วยเป็นมะเร็งในเด็ก (<18 ปี) หรือเป็นชนิดที่หายากคือ

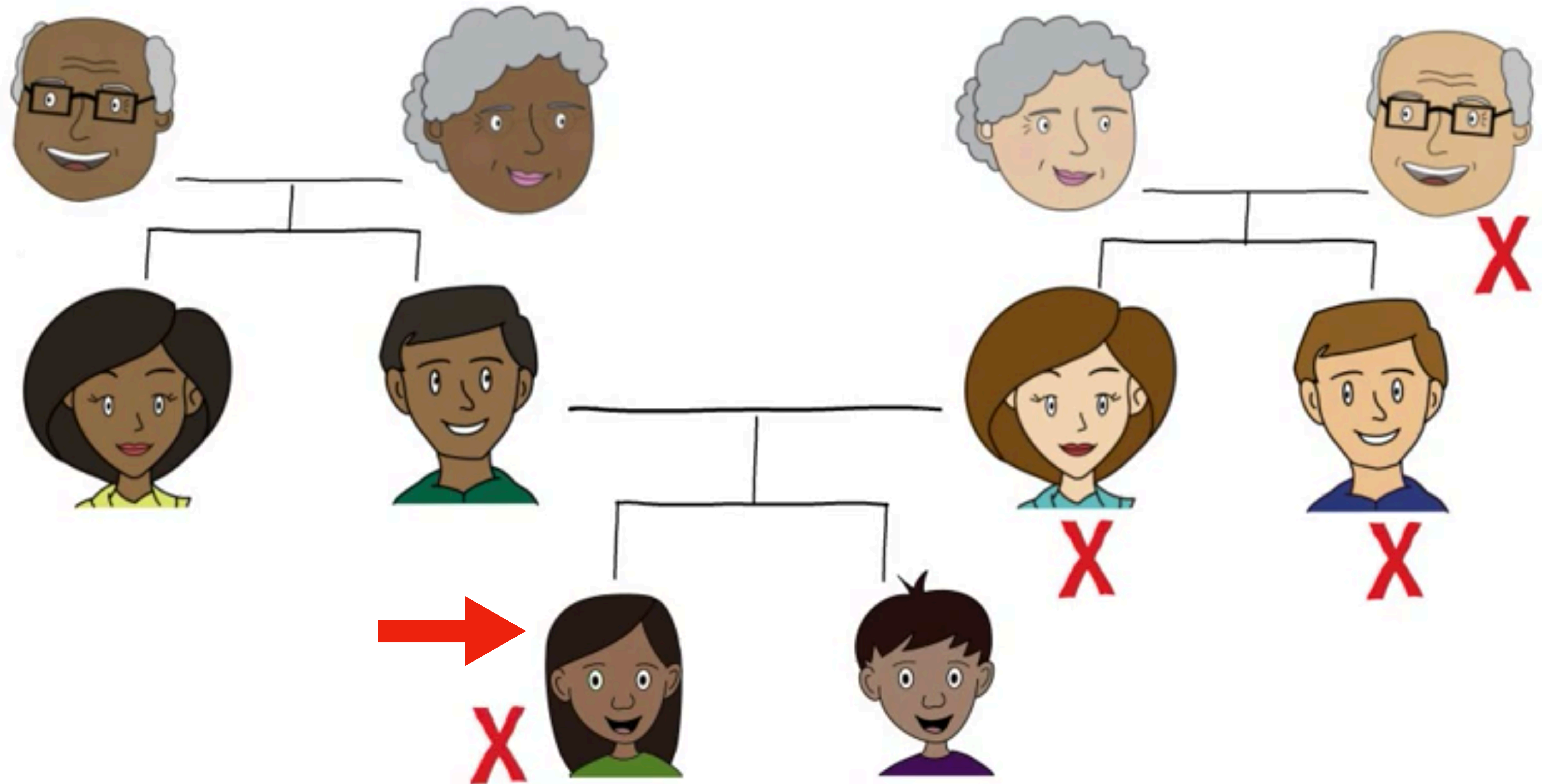
☐ ผู้ป่วยมะเร็งที่มีชิ้นเนื้อมะเร็งเพื่อส่งตรวจ tumor sequencing ในโครงการด้วย

อ้างอิงจาก NCCN Clinical Practice Guidelines in Oncology - Genetic/Familial High-Risk Assessment: Breast & Ovarian and Colorectal Cancers

Latest Update: Breast & Ovarian Version 3/2019, Colorectal Version 2/2019

The National Comprehensive Cancer Network® www.nccn.org

Germline mutation



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Siriraj Genomics Reference
Lab Code: CCP-2637 CN: 645109
Report No. A65-0610-1

TNBC < 60 ปี

HN	DOB	Age	Gender	Specimen Type	Received Date
6405834	06.01.2511	53 yrs	Female	EDTA Blood	24 November 2021

Ordering Physician
นพ.ปรัชญา อินทสุวรรณ

Healthcare Provider
รพ.พระปกเกล้า จันทบุรี

Report Date
14 February 2022

Reason for Testing
Diagnostic testing for hereditary cancer
(Breast cancer)

Test Performed
Core Cancer Panel 36

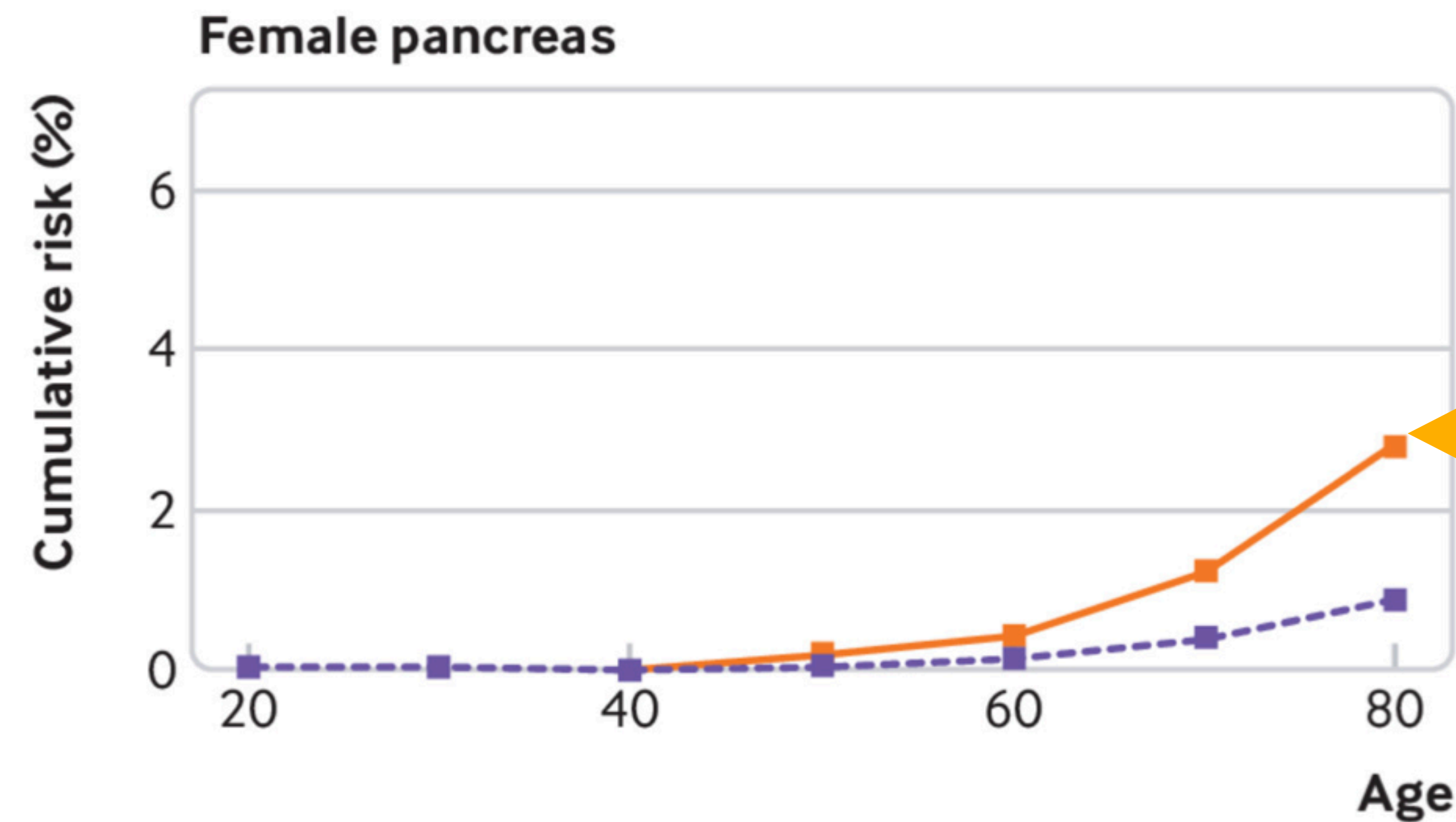
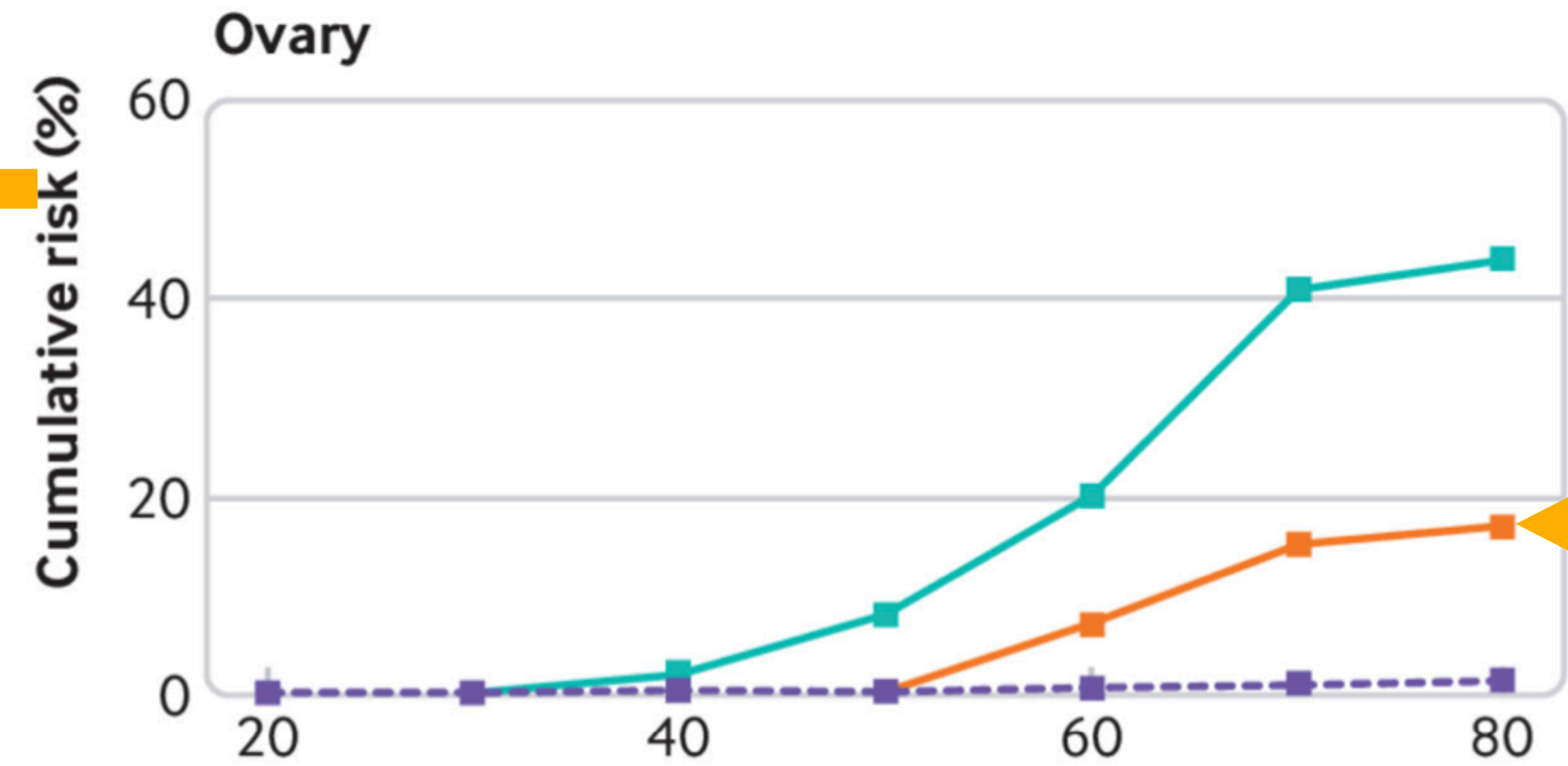
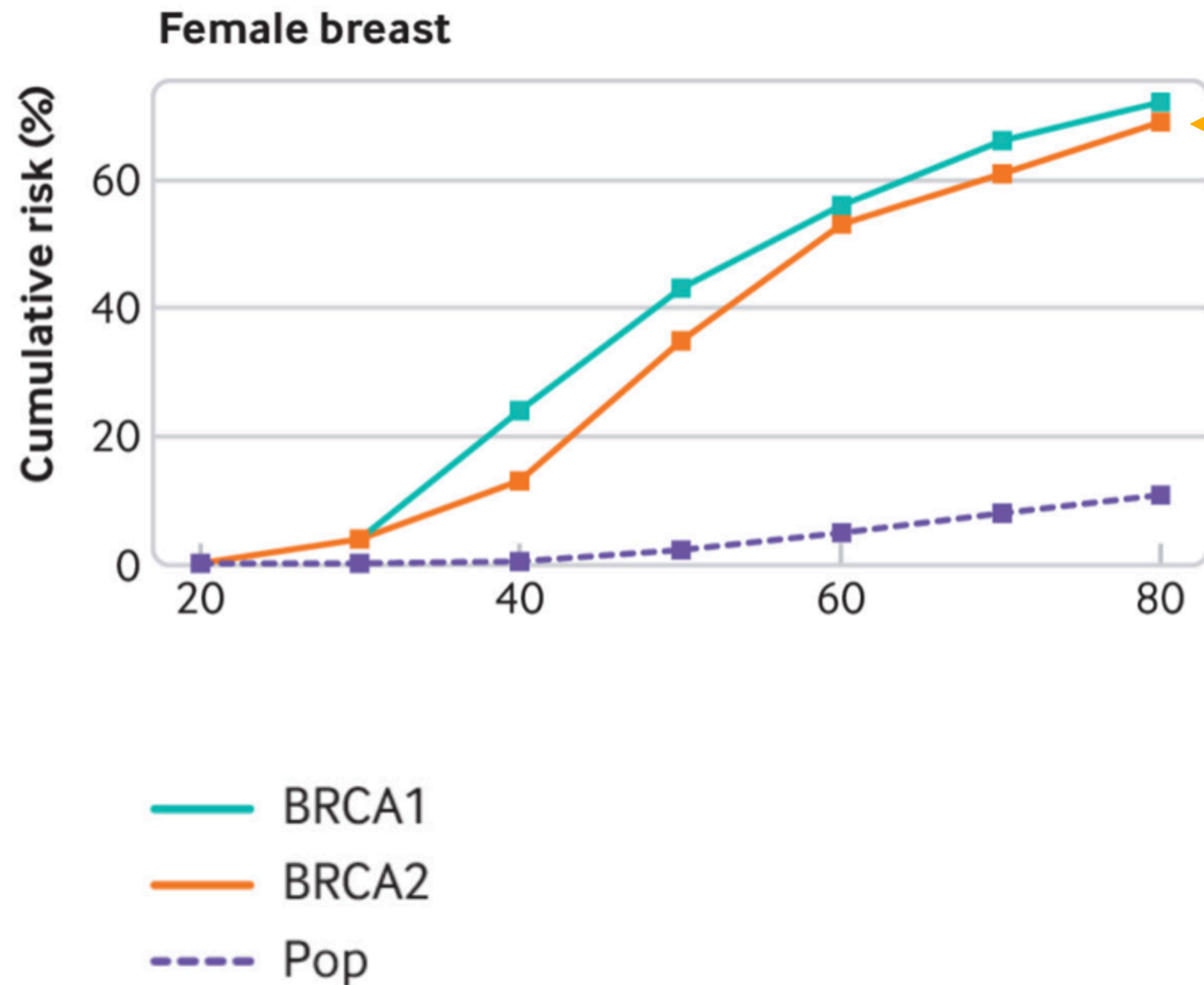
CLINICAL **BRCA2**

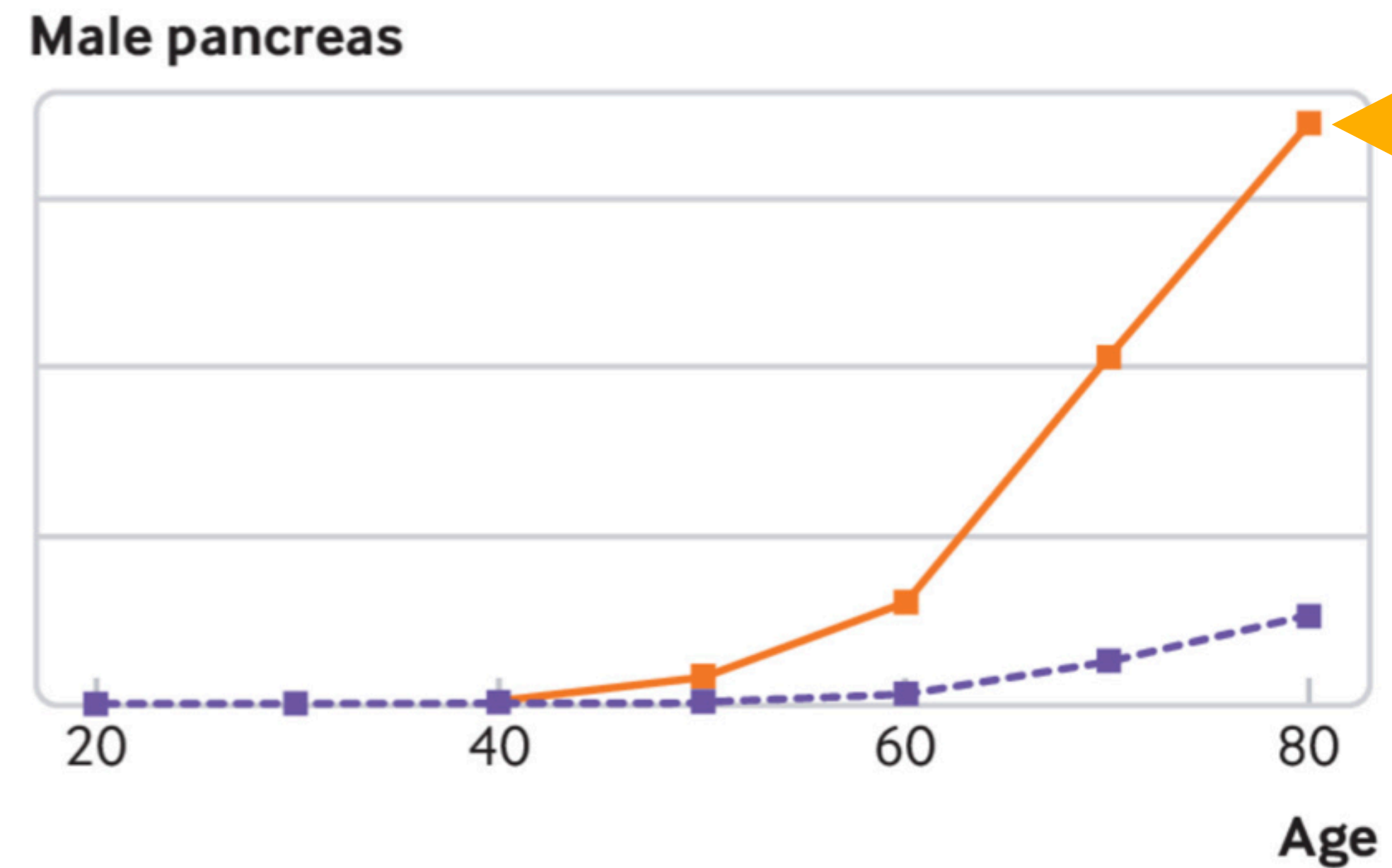
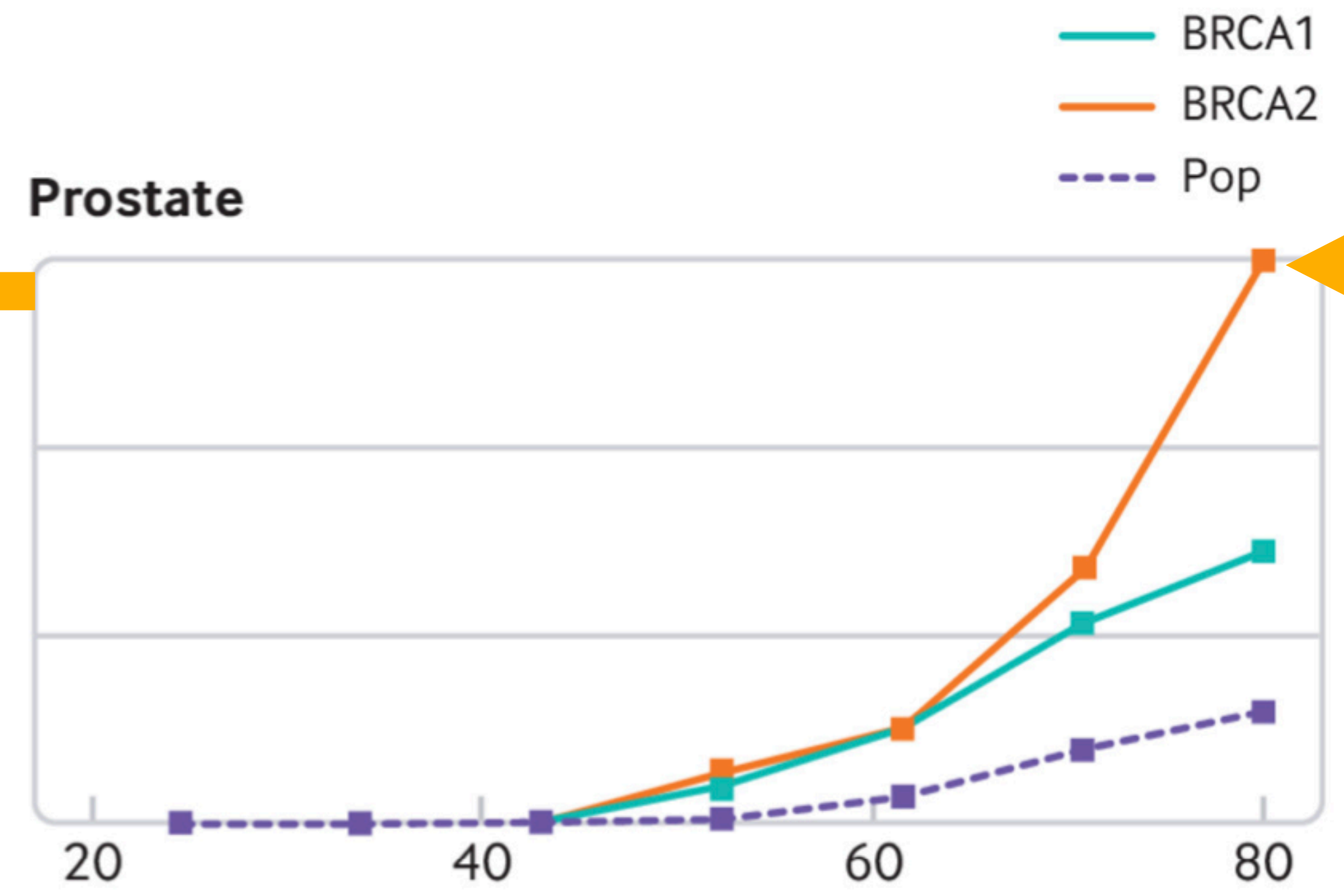
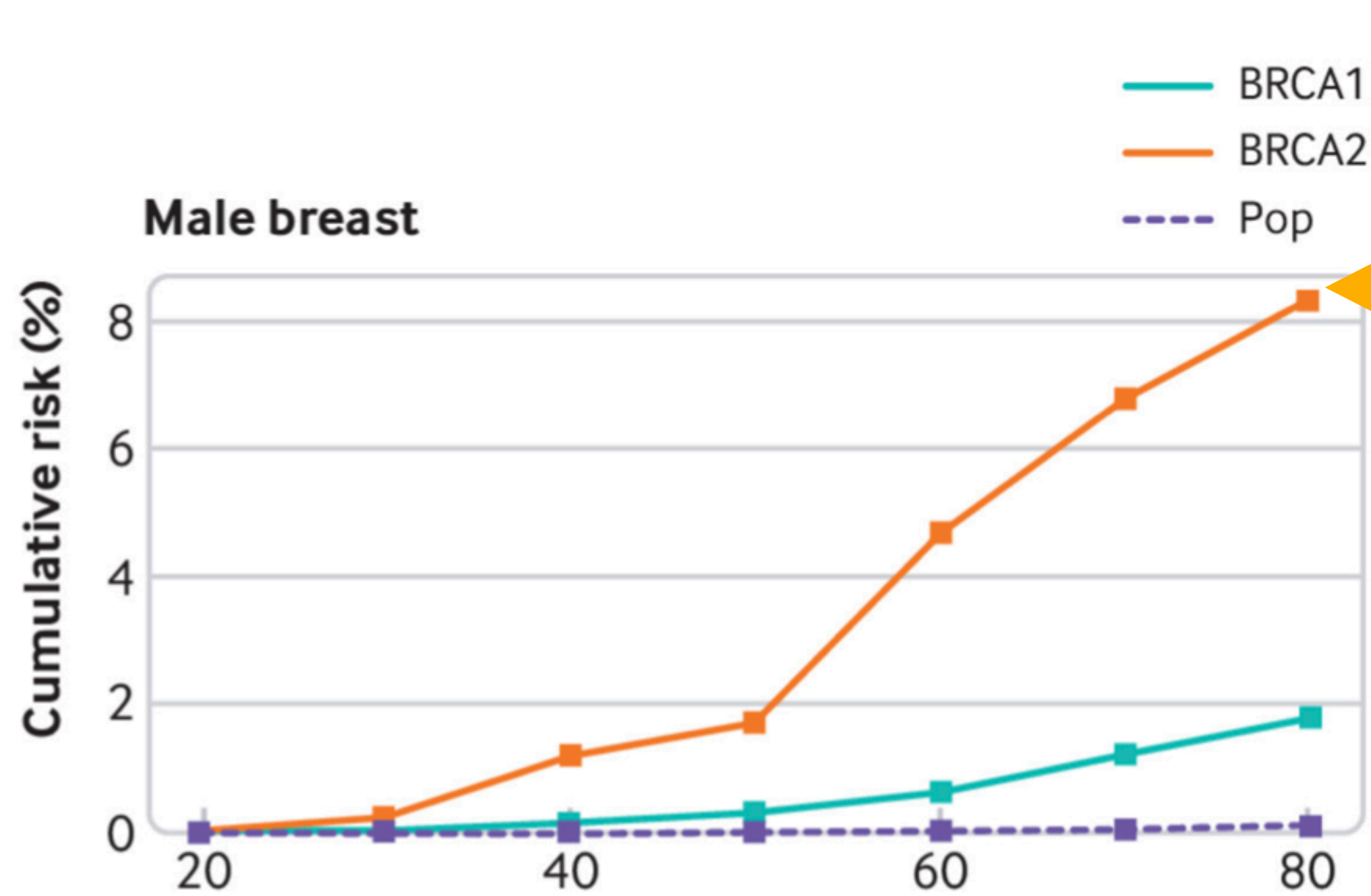
 **Positive** A heterozygous pathogenic variant in *BRCA2* gene (c.2808_2811delACAA, p.Ala938Profs*21) was found, being consistent with a diagnosis of hereditary breast and ovarian cancer (HBOC).
Clinical significance: High cancer risk, autosomal dominant inheritance

Comments: - The results should be interpreted within the context of clinical findings, family history, and additional laboratory results.
- Genetic counseling is recommended to discuss implications of the test result for the patient's relatives and options for targeted testing.

27 ปี

24 ปี





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Siriraj Genomics Reference
Lab Code: CCP-2637 CN: 645109
Report No. **A65-0610-1**

TNBC < 60 ปี

HN	DOB	Age	Gender	Specimen Type	Received Date
6405834	06.01.2511	53 yrs	Female	EDTA Blood	24 November 2021

Ordering Physician: นพ.ปรัชญา อินทสุวรรณ
Healthcare Provider: รพ.พระปกเกล้า จันทบุรี
Report Date: 14 February 2022

Reason for Testing: Diagnostic testing for hereditary cancer (Breast cancer)
Test Performed: Core Cancer Panel 36

CLINICAL **BRCA2**

Positive A heterozygous pathogenic variant in *BRCA2* gene (c.2808_2811delACAA, p.Ala938Profs*21) was found, being consistent with a diagnosis of hereditary breast and ovarian cancer (HBOC).
Clinical significance: High cancer risk, autosomal dominant inheritance

Comments: - The results should be interpreted within the context of clinical findings, family history, and additional laboratory results.
- Genetic counseling is recommended to discuss implications of the test result for the patient's relatives and options for targeted testing.

27 ปี

Patient Name	HN	DOB	Age	Gender	Specimen Type	Received Date
	6538039	16.08.2538	27 yrs	Male	EDTA Blood	23 November 2022

Healthcare Provider: รพ.พระปกเกล้า จันทบุรี
Report Date: 07 December 2022

Reason for Testing: Targeted-variant testing for NM_000059.4[*BRCA2*]:c.2808_2811delACAA, p.Ala938Profs*21 (found in his mother affected with breast cancer)
Test Performed: Sanger Sequencing

CLINICAL INTERPRETATION **BRCA2**

Positive Presence of the heterozygous pathogenic germline variant (*BRCA2*: c.2808_2811delACAA, p.Ala938Profs*21) predisposes this individual to hereditary breast and ovarian cancer (HBOC) syndrome.
Clinical significance: Autosomal dominant inheritance, high cancer risk

Comments: 1. This test method detected only the specified variant.
2. This test results and interpretation are based on current knowledge and technology.
3. Genetic counseling is recommended to discuss the implications of the genetic test result for this individual's relatives and options for targeted testing.

24 ปี

Patient Name	HN	DOB	Age	Gender	Specimen Type	Received Date
	6538041	15.07.2541	24 yrs	Male	EDTA Blood	23 November 2022

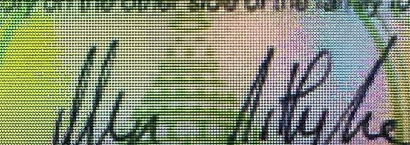
Healthcare Provider: รพ.พระปกเกล้า จันทบุรี
Report Date: 07 December 2022

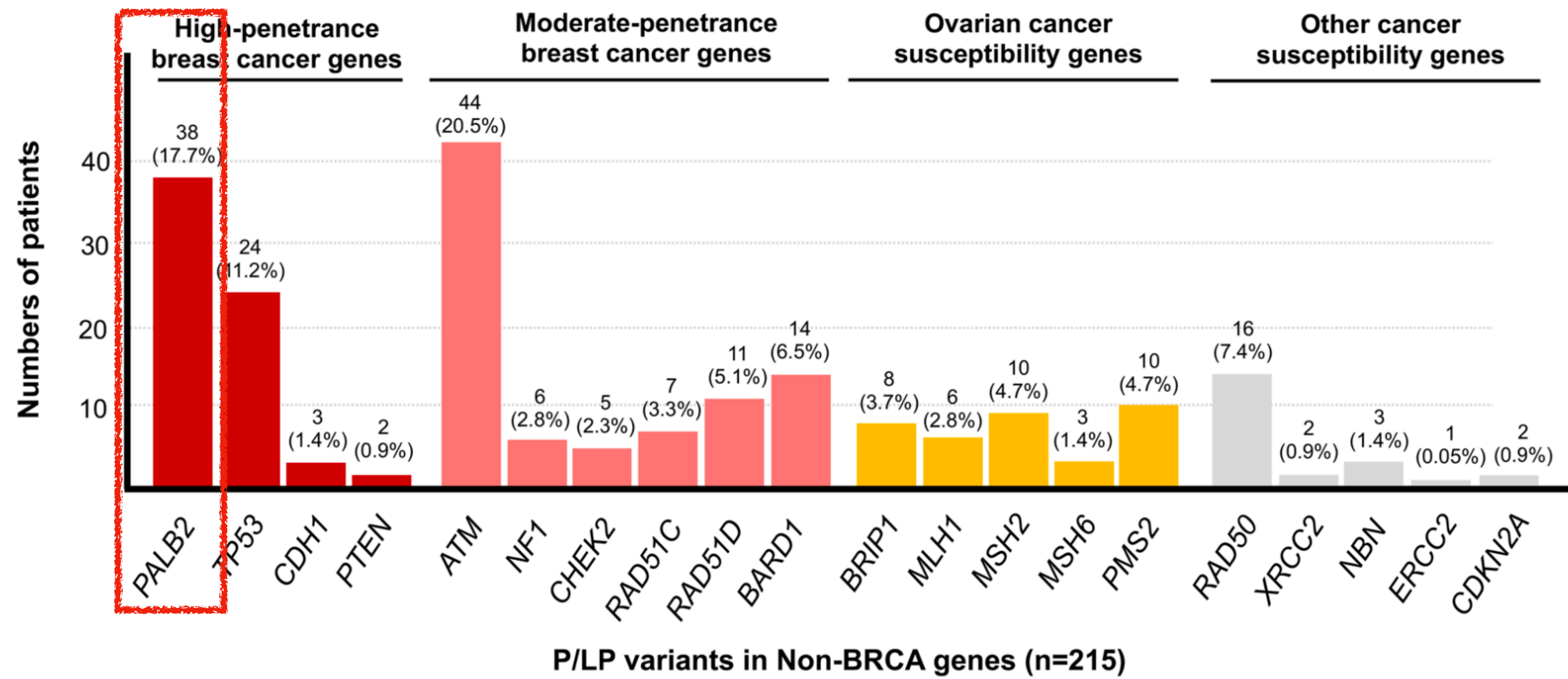
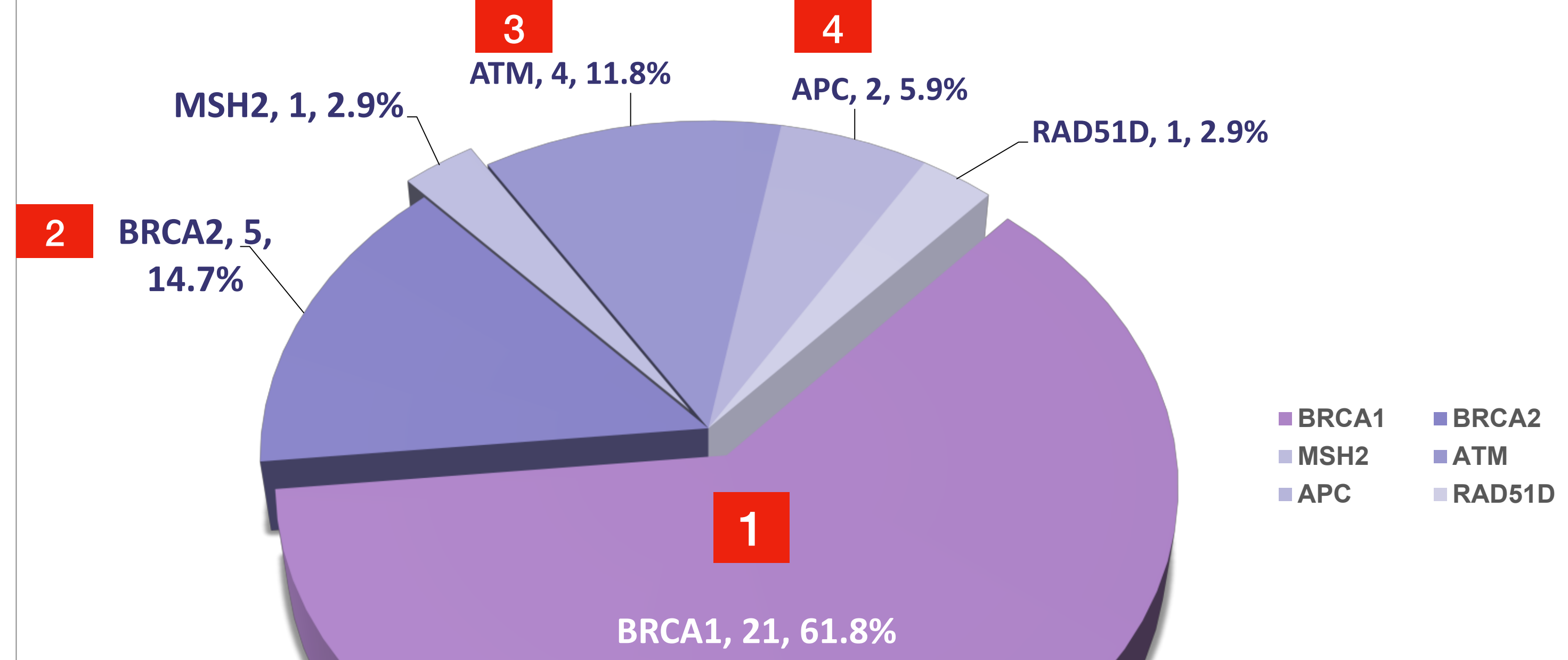
Reason for Testing: Targeted-variant testing for NM_000059.4[*BRCA2*]:c.2808_2811delACAA, p.Ala938Profs*21 (found in his mother affected with breast cancer)
Test Performed: Sanger Sequencing

CLINICAL INTERPRETATION **No BRCA2**

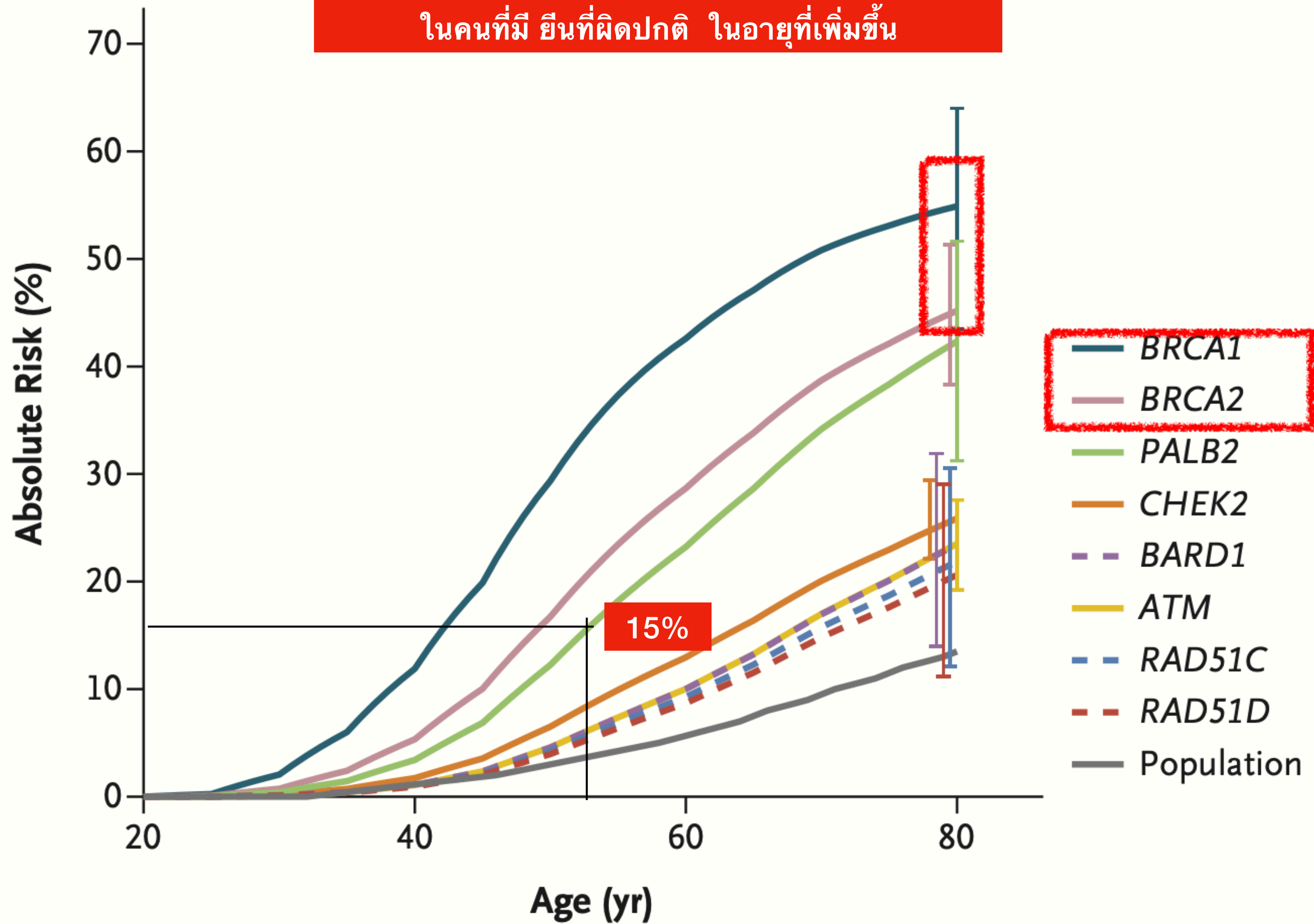
Negative Absence of the specified pathogenic germline variant (*BRCA2*: c.2808_2811delACAA, p.Ala938Profs*21)

Comments: 1. This test method detected only the specified variant.
2. This test results and interpretation are based on current knowledge and technology.
3. Genetic counseling is recommended to discuss the implications of the genetic test result.
4. Regarding an absence of the specified *BRCA2* mutation in this individual, he can be reassured that his risk of HBOC is no greater than that of the general population (assuming that there is no history on the other side of the family for a hereditary cancer and that there are no other risk factors).

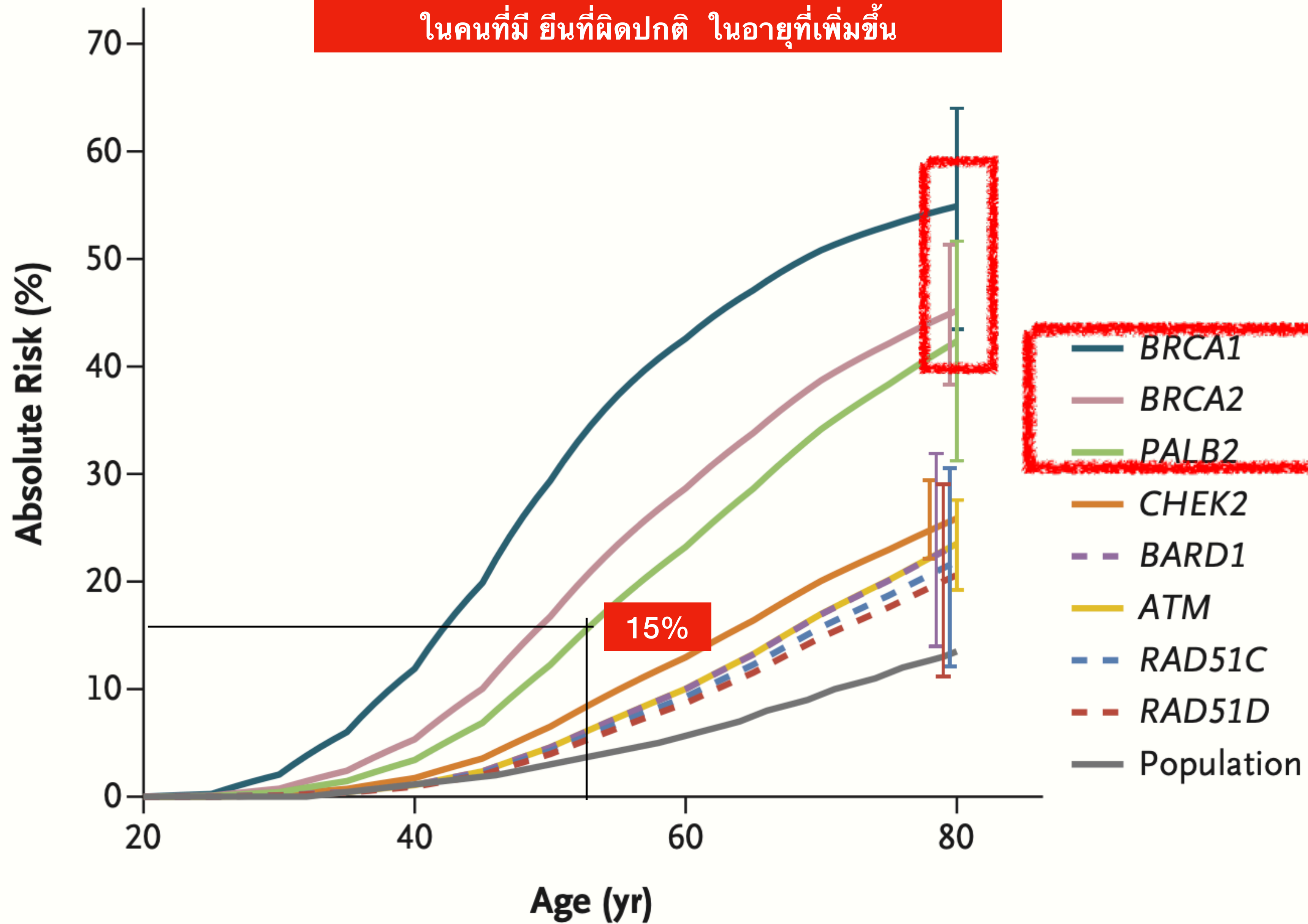
This report has been reviewed and approved by:  (Manop Pithukpakorn, M.D., ABMG)



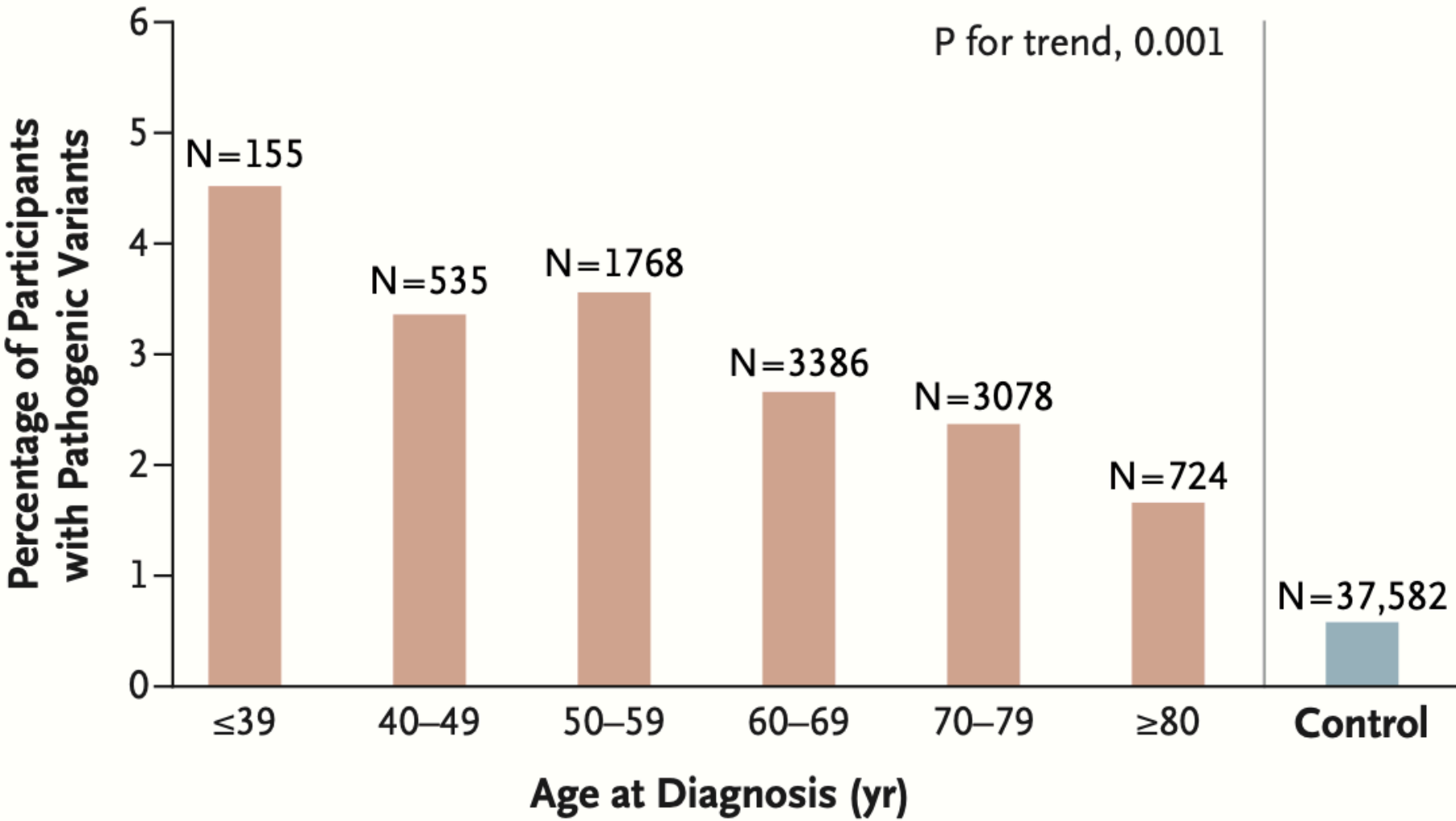
ความเสี่ยงของการเกิด มะเร็งเต้านม
ในคนที่มี ยีนที่ผิดปกติ ในอายุที่เพิ่มขึ้น



ความเสี่ยงของการเกิด มะเร็งเต้านม
ในคนที่มี ยีนที่ผิดปกติ ในอายุที่เพิ่มขึ้น



A Percentages of Patients with Gastric Cancer Who Are Carriers of Pathogenic Variants, According to Age at Diagnosis



B Age at Diagnosis among Carriers of Pathogenic Variants, According to Gene

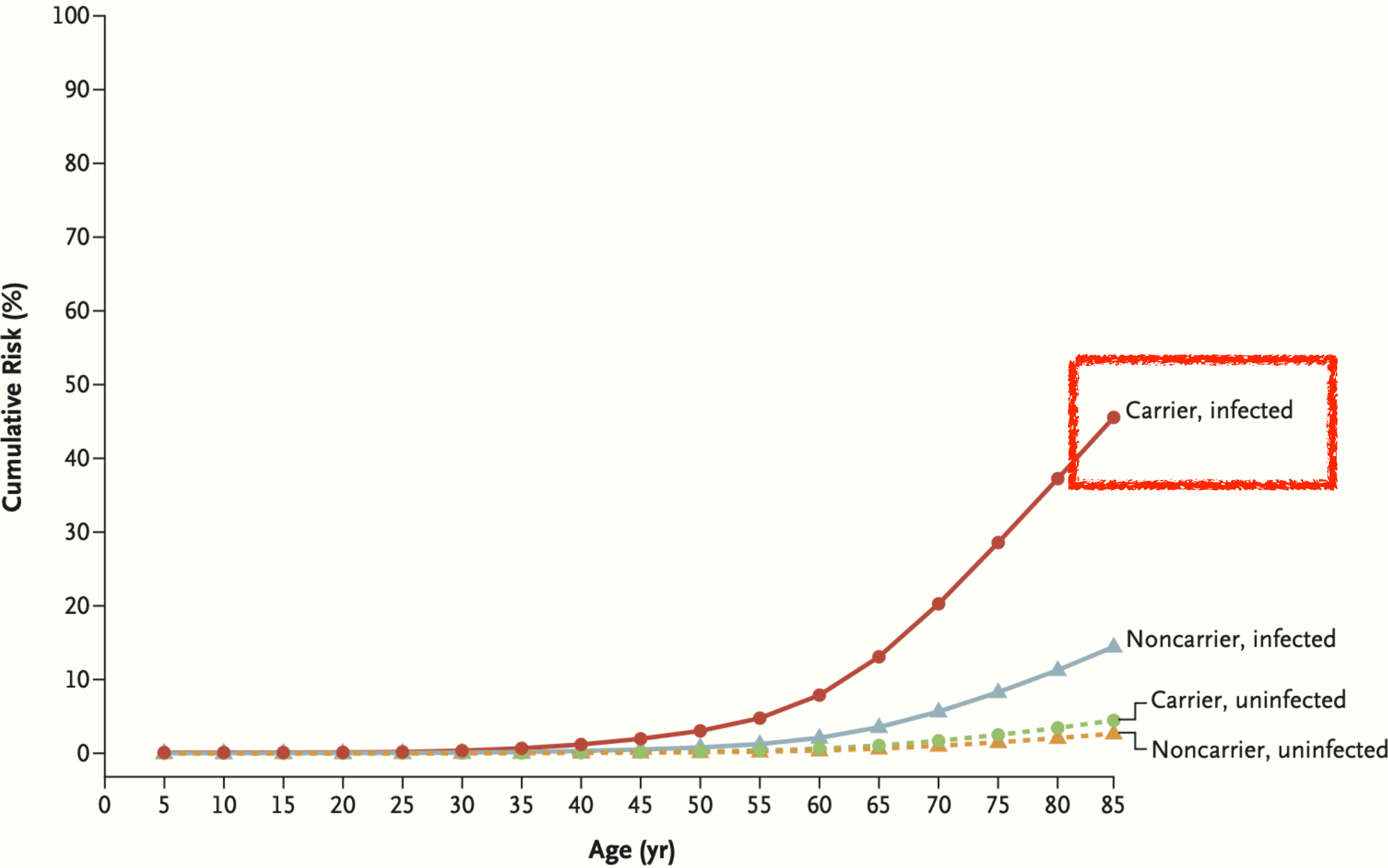
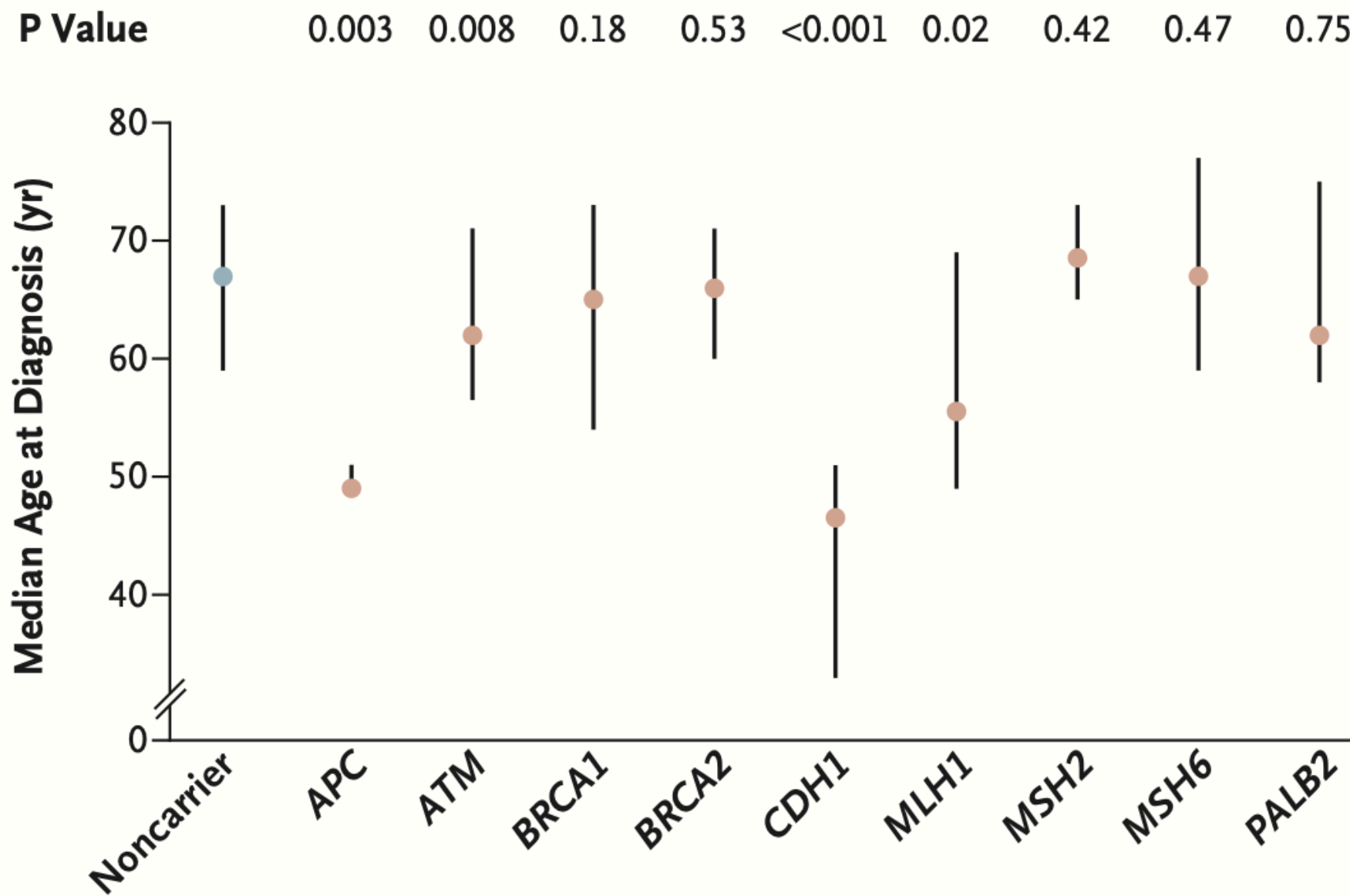


Figure 2. Cumulative Risk of Gastric Cancer through 85 Years of Age According to Germline Pathogenic-Variant Carrier Status and *Helicobacter pylori* Infection Status.

Cumulative risks of gastric cancer were estimated for carriers and noncarriers of germline pathogenic variants and persons who were positive and negative for *H. pylori* infection in the Hospital-based Epidemiologic Research Program at Aichi Cancer Center. Noncarriers were defined as persons without pathogenic variants in gastric cancer risk genes (*APC*, *ATM*, *BRCA1*, *BRCA2*, *CDH1*, *MLH1*, *MSH2*, *MSH6*, and *PALB2*). Only carriers of pathogenic variants in homologous-recombination (HR) genes (*ATM*, *BRCA1*, *BRCA2*, and *PALB2*) are shown in this figure because of the limited number of participants with variants in non-HR genes (*APC*, *CDH1*, *MLH1*, *MSH2*, and *MSH6*).

ORIGINAL ARTICLE

Helicobacter pylori, Homologous-Recombination Genes, and Gastric Cancer

Yoshiaki Usui, M.D., Ph.D., Yukari Taniyama, Ph.D., Mikiko Endo, B.Sc.,
Yuriko N. Koyanagi, M.D., Ph.D., Yumiko Kasugai, M.M.Sc.,
Isao Oze, M.D., Ph.D., Hidemi Ito, M.D., Ph.D., M.P.H., Issei Imoto, M.D., Ph.D.,
Tsutomu Tanaka, M.D., Ph.D., Masahiro Tajika, M.D., Ph.D.,
Yasumasa Niwa, M.D., Ph.D., Yuriko Iwaseki, M.F., Tamagari Aoi, B.Sc.



NCCN Guidelines Version 1.2022

BRCA-Pathogenic/Likely Pathogenic Variant - Positive Management

BRCA PATHOGENIC/LIKELY PATHOGENIC VARIANT-POSITIVE MANAGEMENT

GENERAL

- Education regarding signs and symptoms of cancer(s), especially those associated with *BRCA* gene pathogenic/likely pathogenic variants.

BREAST CANCER

• Female

- ▶ Breast awareness^a starting at age 18 years.
 - ▶ Clinical breast exam, every 6–12 months,^b starting at age 25 years.
 - ▶ Breast screening^{c,d}
 - ◇ Age 25–29 years, annual breast MRI^e screening with contrast^f (or mammogram with consideration of tomosynthesis, only if MRI is unavailable) or individualized based on family history if a breast cancer diagnosis before age 30 is present.
 - ◇ Age 30–75 years, annual mammogram with consideration of tomosynthesis and breast MRI^e screening with contrast.
 - ◇ Age >75 years, management should be considered on an individual basis.
 - ◇ For individuals with a *BRCA* pathogenic/likely pathogenic variant who are treated for breast cancer and have not had a bilateral mastectomy, screening with annual mammogram with consideration of tomosynthesis and breast MRI should continue as described above.
 - ▶ Discuss option of risk-reducing mastectomy
 - ◇ Counseling should include a discussion regarding degree of protection, reconstruction options, and risks. In addition, the family history and residual breast cancer risk with age and life expectancy should be considered during counseling.
 - ▶ Address psychosocial and quality-of-life aspects of undergoing risk-reducing mastectomy.
- Consider risk reduction agents as options for breast cancer, including discussion of risks and benefits ([See Discussion](#) for details). ([See NCCN Guidelines for Breast Cancer Risk Reduction](#)).

• Male

- ▶ Breast self-exam training and education starting at age 35 years.
- ▶ Clinical breast exam, every 12 months, starting at age 35 years.
- ▶ Consider annual mammogram screening in men with gynecomastia starting at age 50 or 10 years before the earliest known male breast cancer in the family (whichever comes first).^g



NCCN Guidelines Version 1.2022

BRCA-Pathogenic/Likely Pathogenic Variant - Positive Management

BRCA PATHOGENIC/LIKELY PATHOGENIC VARIANT-POSITIVE MANAGEMENT

OVARIAN/UTERINE CANCER

- **Recommend risk-reducing salpingo-oophorectomy (RRSO),^h typically between 35 and 40 years, and upon completion of childbearing. Because ovarian cancer onset in patients with *BRCA2* pathogenic/likely pathogenic variants is an average of 8–10 years later than in patients with *BRCA1* pathogenic/likely pathogenic variants, it is reasonable to delay RRSO for management of ovarian cancer risk until age 40–45 years in patients with *BRCA2* pathogenic/likely pathogenic variants unless age at diagnosis in the family warrants earlier age for consideration of prophylactic surgery. See Risk-Reducing Salpingo-Oophorectomy (RRSO) Protocol in [NCCN Guidelines for Ovarian Cancer](#) - Principles of Surgery.**
 - ▶ Counseling includes a discussion of reproductive desires, extent of cancer risk, degree of protection for breast and ovarian cancer, management of menopausal symptoms, hormone replacement therapy, and related medical issues.
 - ▶ Salpingectomy alone is not the standard of care for risk reduction, although clinical trials of interval salpingectomy and delayed oophorectomy are ongoing. The concern for risk-reducing salpingectomy alone is that individuals are still at risk for developing ovarian cancer. In addition, in premenopausal individuals, oophorectomy likely reduces the risk of developing breast cancer but the magnitude is uncertain and may be gene-specific.
- Limited data suggest that there may be a slightly increased risk of serous uterine cancer among individuals with a *BRCA1* pathogenic/likely pathogenic variant. The clinical significance of these findings is unclear. Further evaluation of the risk of serous uterine cancer in the *BRCA* population needs to be undertaken. The provider and patient should discuss the risks and benefits of concurrent hysterectomy at the time of RRSO for individuals with a *BRCA1* pathogenic/likely pathogenic variant prior to surgery.
- Individuals who undergo hysterectomy at the time of RRSO are candidates for estrogen-alone hormone replacement therapy, which is associated with a decreased risk of breast cancer compared to combined estrogen and progesterone, which is required when the uterus is left in situ (Chlebowski R, et al. JAMA Oncol 2015;1:296-305).
- Address psychosocial and quality-of-life aspects of undergoing RRSO.
- For those patients who have not elected RRSO, transvaginal ultrasound combined with serum CA-125 for ovarian cancer screening, although of uncertain benefit, may be considered at the clinician's discretion starting at age 30–35 y.
- Consider risk reduction agents as options for ovarian cancer, including discussion of risks and benefits ([See Discussion](#) for details).



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BRCA-Pathogenic/Likely Pathogenic Variant - Positive Management

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BRCA PATHOGENIC/LIKELY PATHOGENIC VARIANT-POSITIVE MANAGEMENT

PANCREATIC CANCER

- For pancreatic cancer screening recommendations, [see PANC-A](#).

PROSTATE CANCER

- **Starting at age 40 years:** ([See Guidelines for Prostate Cancer Early Detection](#))
 - ▶ Recommend prostate cancer screening for **BRCA2** carriers.
 - ▶ Consider prostate cancer screening for **BRCA1** carriers.

MELANOMA

- No specific screening guidelines exist for melanoma, but general melanoma risk management is appropriate, such as annual full-body skin examination and minimizing UV exposure.

RISK TO RELATIVES

- [Principles of Cancer Risk Assessment and Counseling \(EVAL-A\)](#)

REPRODUCTIVE OPTIONS

- [Principles of Cancer Risk Assessment and Counseling \(EVAL-A\)](#)



PANCREATIC CANCER SCREENING

- For individuals considering pancreatic cancer screening, the panel recommends that screening be performed in experienced high-volume centers. The panel recommends that such screening only take place after an in-depth discussion about the potential limitations to screening, including cost, the high incidence of benign or indeterminate pancreatic abnormalities, and uncertainties about the potential benefits of pancreatic cancer screening.
- Consider screening using annual contrast-enhanced MRI/MRCP and/or EUS, with consideration of shorter screening intervals, based on clinical judgment, for individuals found to have potentially concerning abnormalities on screening. The panel emphasizes that most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any other intervention.
- For all individuals with pathogenic/likely pathogenic germline variants in *STK11*
 - ▶ Consider pancreatic cancer screening beginning at age 30–35 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family, whichever is earlier).
- For all individuals with pathogenic/likely pathogenic germline variants in *CDKN2A*
 - ▶ Consider pancreatic cancer screening beginning at age 40 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family, whichever is earlier).
- For individuals with pathogenic/likely pathogenic germline variants in one of the other pancreatic cancer susceptibility genes (*ATM*, *BRCA1*, *BRCA2*, *MLH1*, *MSH2*, *MSH6*, *EPCAM*, *PALB2*, *TP53*), [see GENE-A](#).
 - ▶ Consider pancreatic cancer screening beginning at age 50 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family, whichever is earlier) for individuals with exocrine pancreatic cancer in ≥1 first- or second-degree relatives from the same side of (or presumed to be from the same side of) the family as the identified pathogenic/likely pathogenic germline variant.^d
 - ▶ The panel does not currently recommend pancreatic cancer screening for carriers of mutations in genes other than *STK11* and *CDKN2A* in the absence of a close family history of exocrine pancreatic cancer.

Hereditary Pancreatitis Genes

- For individuals with pathogenic/likely pathogenic variants in *PRSS1* or other hereditary pancreatitis genes AND a clinical phenotype consistent with hereditary pancreatitis^e
 - ▶ Consider pancreatic cancer screening 20 years after onset of pancreatitis, or at age 40 years, whichever is earlier.

leading Cancer in Thailand

9

Figure C Leading cancer in Thailand (mean annual ASR 2016-2018)

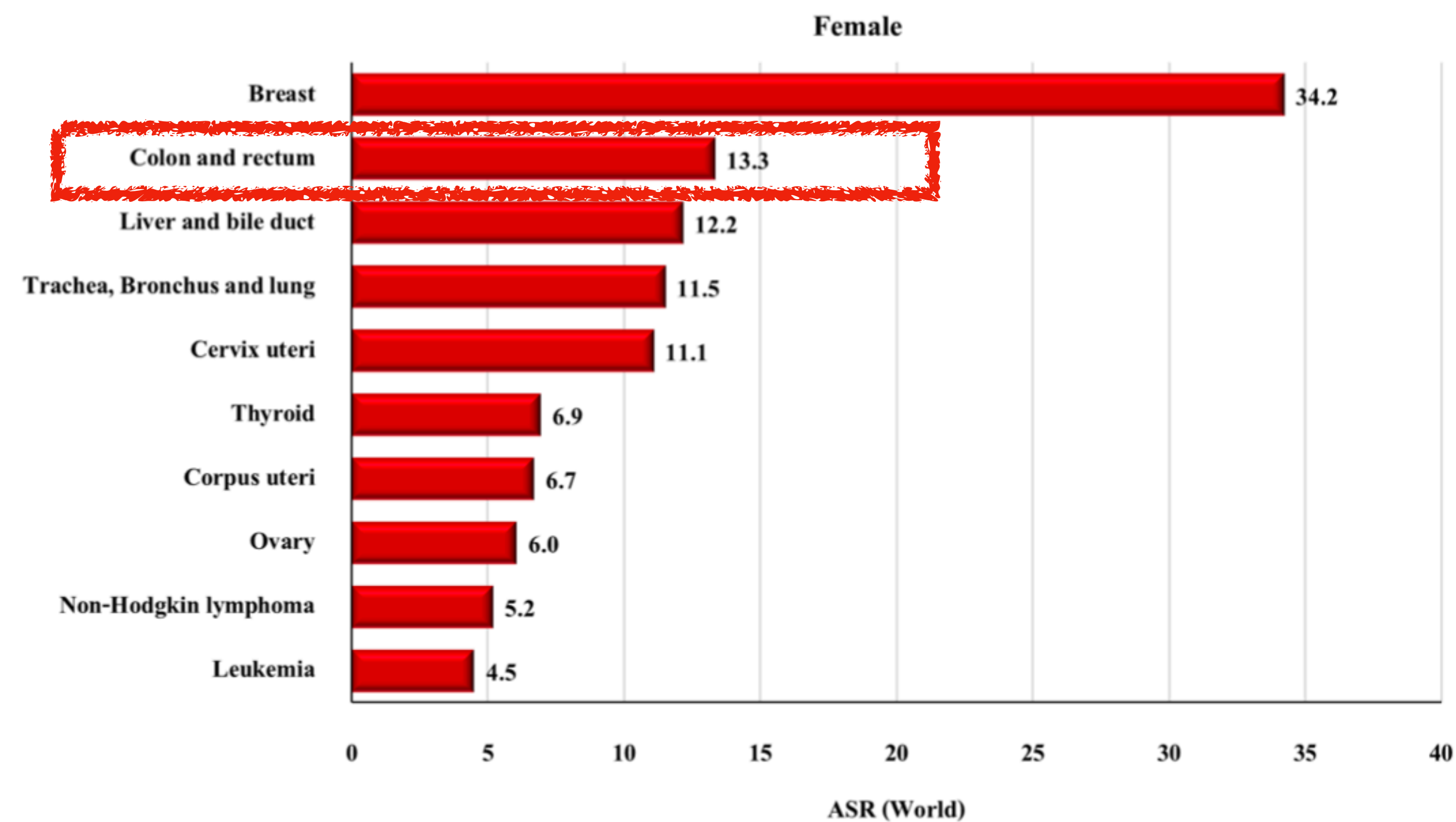
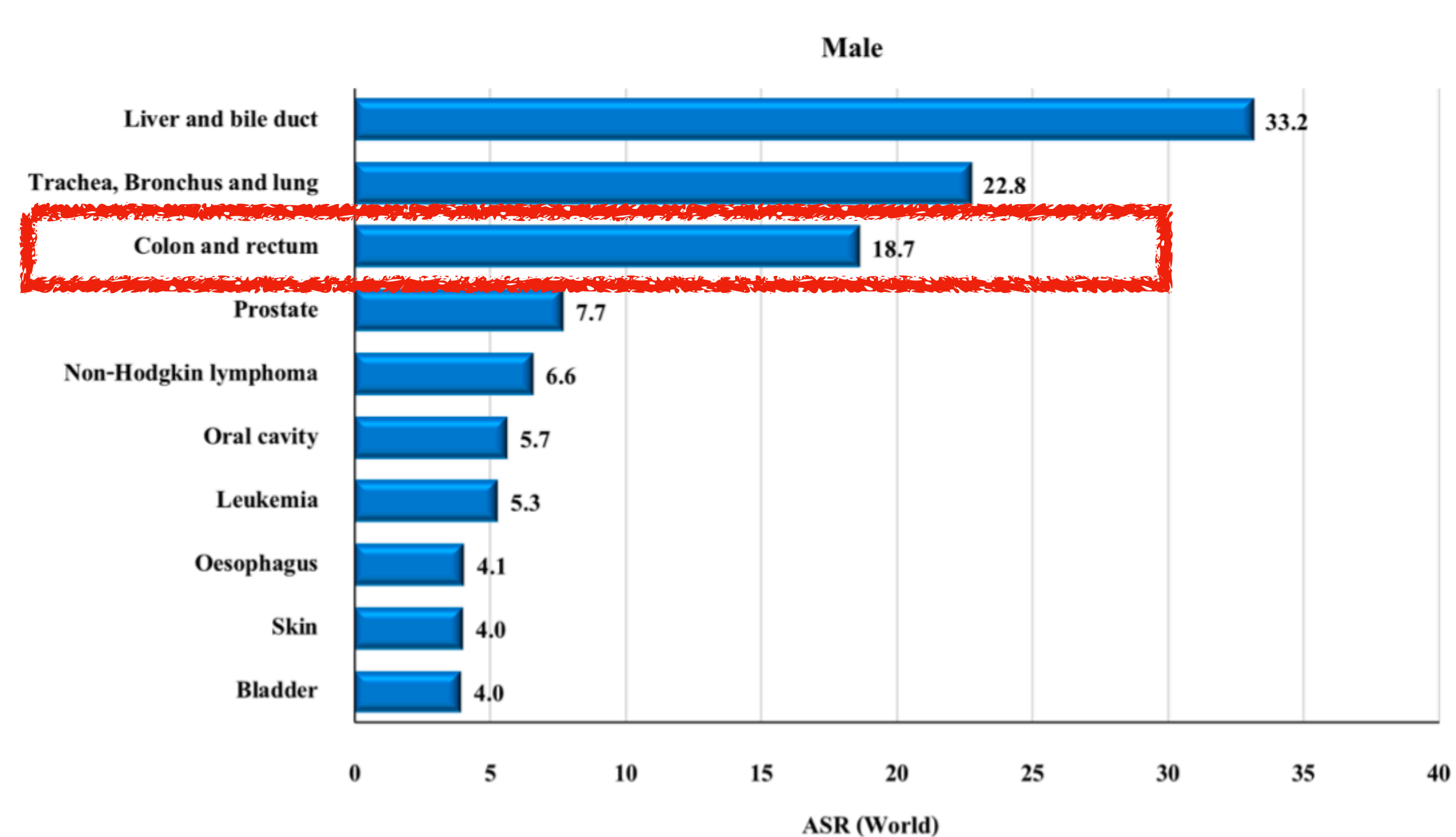
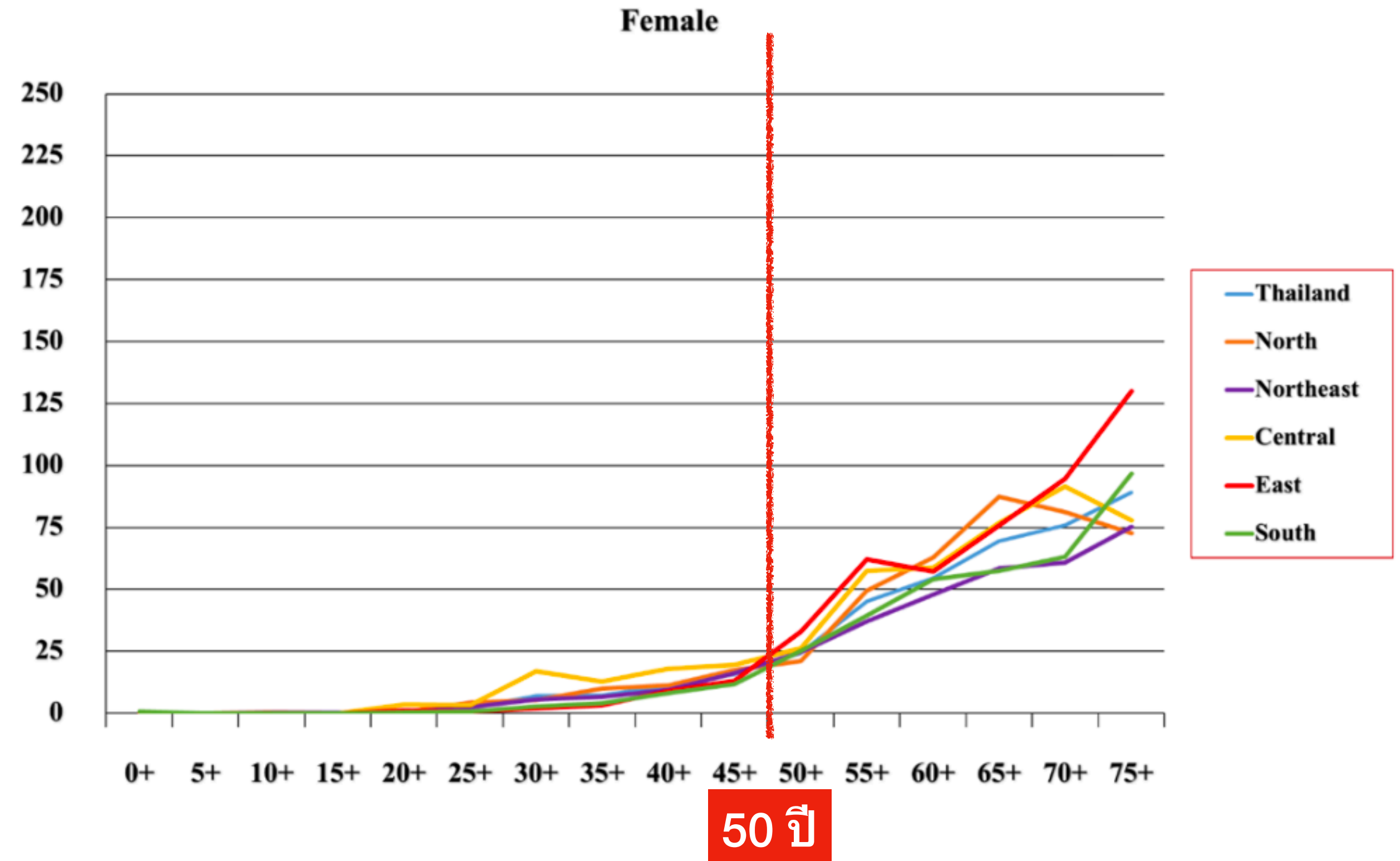
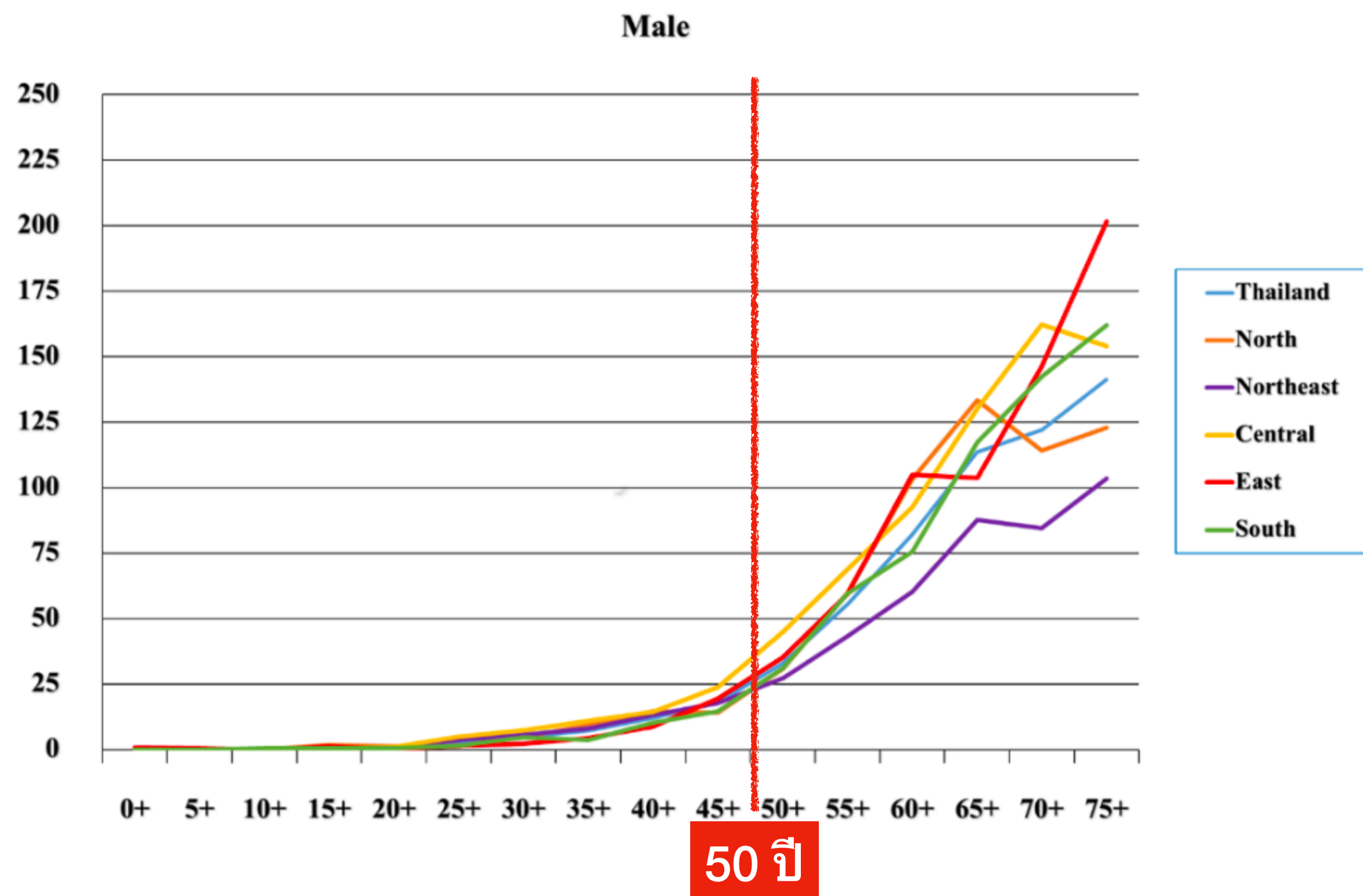
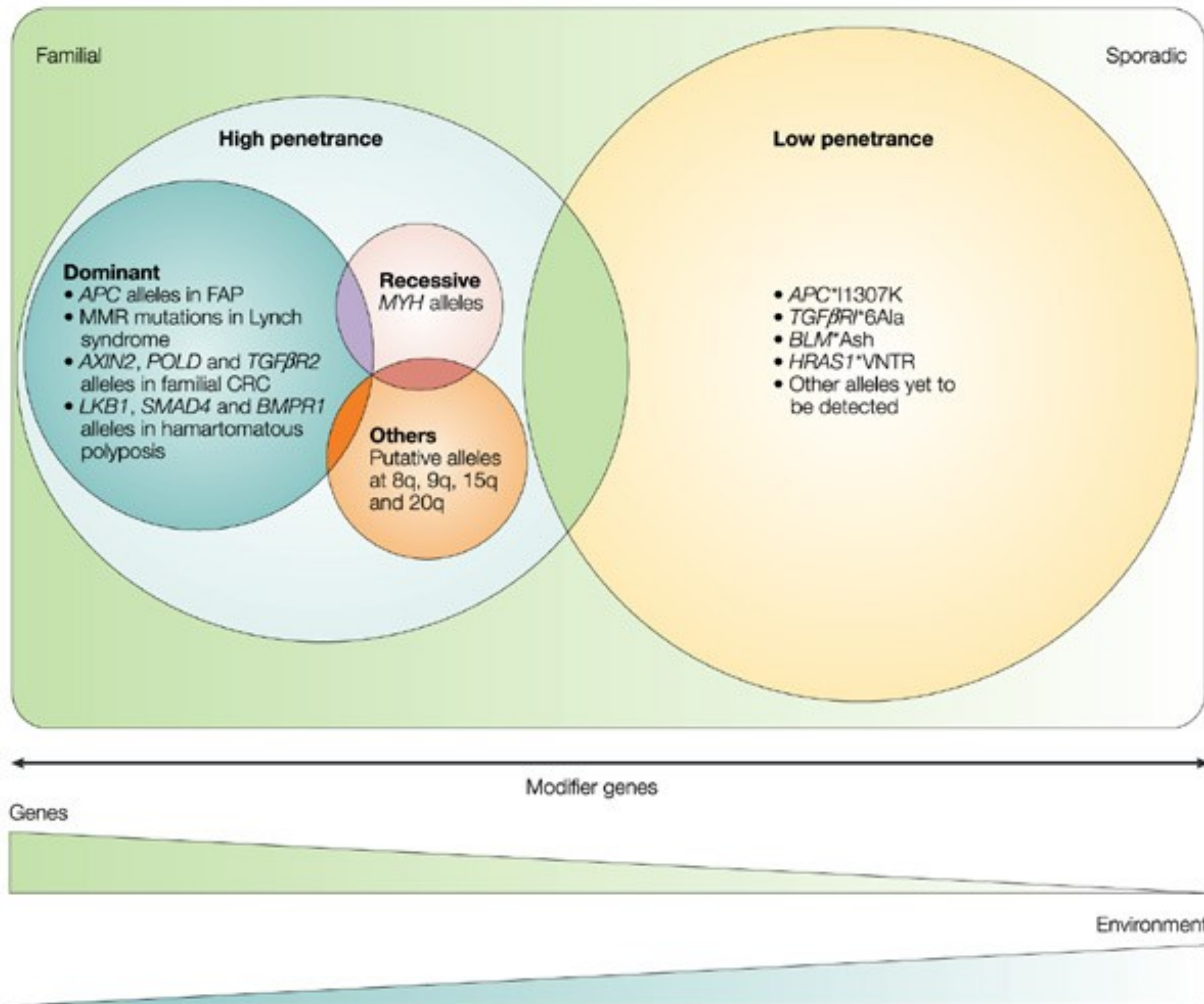


Figure 2.7.2 Age - specific incidence rates of colon and rectum cancer, mean annual rate per 100,000 (2016-2018)





Lynch Syndrome Pedigree

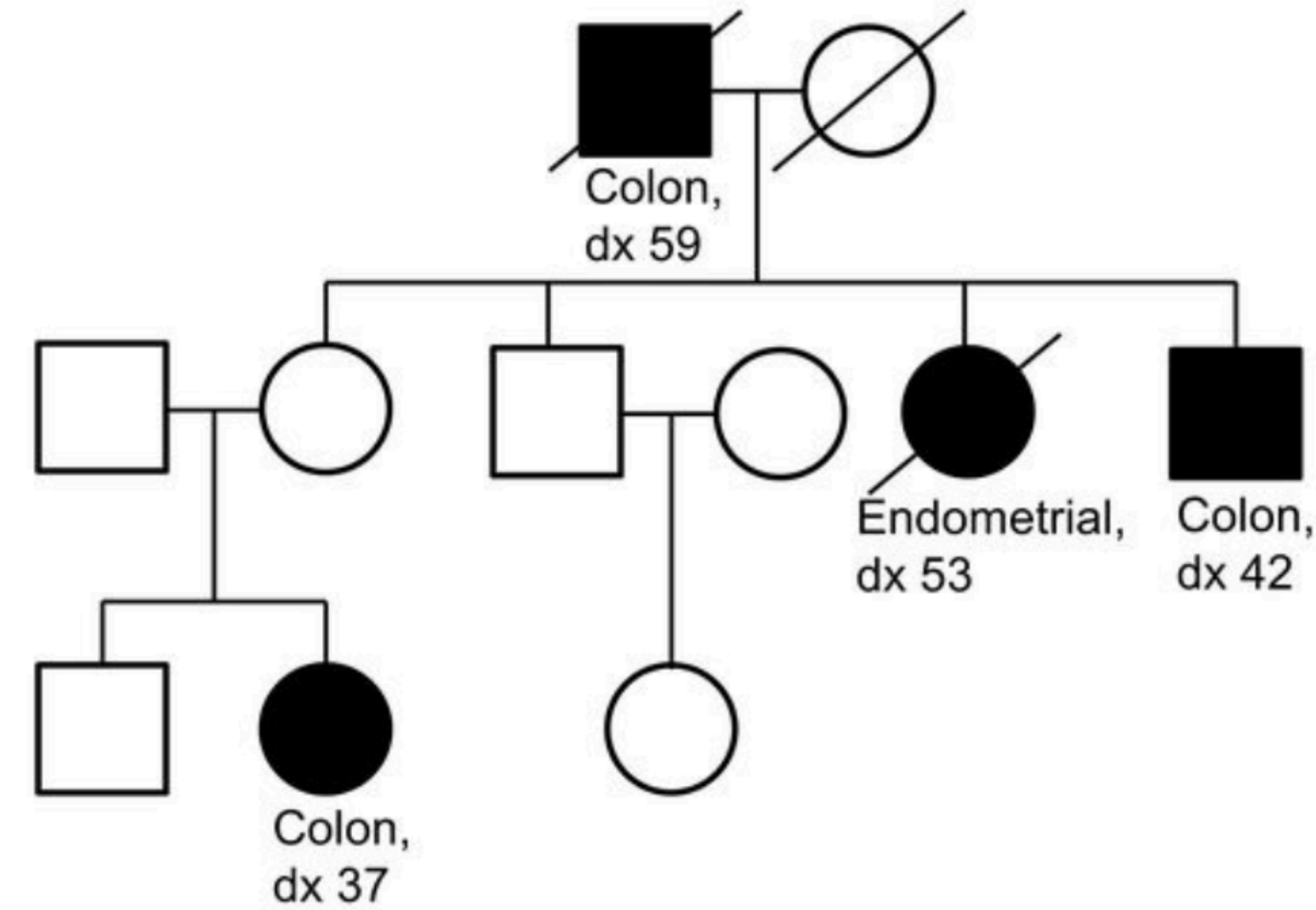


Figure 2. Lynch syndrome pedigree. This pedigree shows some of the classic features of a family with Lynch syndrome, including affected family members with colon cancer or endometrial cancer, a young age at onset in some individuals, and incomplete penetrance. Lynch syndrome families may exhibit some or all of these features. Lynch syndrome families may also include individuals with other gastrointestinal, gynecologic, and genitourinary cancers, or other extracolonic cancers. As an autosomal dominant syndrome, Lynch syndrome can be transmitted through maternal or paternal lineages, as depicted in the figure. Because the cancer risk is not 100%, individuals who have Lynch syndrome may not develop cancer, such as the mother of the female with colon cancer diagnosed at age 37 years in this pedigree (called incomplete penetrance).

Surveillance/Screening Test

Start	Test	Interval	Stop
≥ 40 Y	Mammogram	1 Y	As long as healthy
average risk ≥ 45 Y	FOBT Sigmoidoscopy Colonoscopy	1 Y 5 Y 10 Y	As long as healthy
High risk 55-74 Y	Low dose CT	1 Y x 3	> 74 Y
≥ 21 Y or 3 Y หลังจากเริ่มมีเพศสัมพันธ์ ครั้งแรก	PV + PAP HPV DNA	3 Y 5 Y	> 65 Y
≥ 50 Y with life expectancy ≥ 10 Y	PSA	1 Y	As long as healthy
High risk	AFP + U/S liver	6 m	No data



MLH1 LYNCH SYNDROME: CANCER RISKS^a

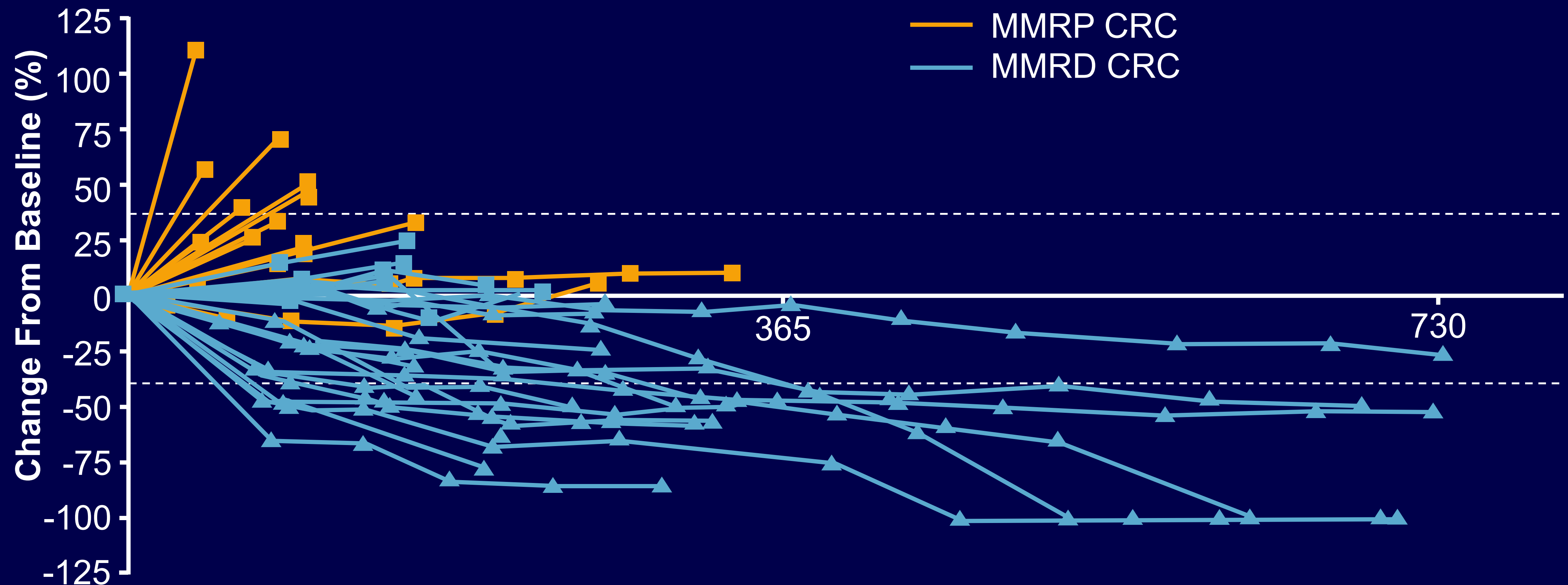
Site	Estimated Average Age of Presentation	Cumulative Risk for Diagnosis Through Age 80 y ^b	Cumulative Risk for Diagnosis Through Lifetime for General Population ^c	Comments and References
Colorectal	44 years	46%–61% ^d	4.2%	See footnote f References 1, 2, 3
Endometrial	49 years	34%–54%	3.1%	References 1, 4
Ovarian	46 years	4%–20%	1.3%	References 1, 5
Renal pelvis and/or ureter	59–60 years	0.2%–5%	— ^e	See footnote g References 1, 2, 5, 6, 7
Bladder	59 years	2%–7%	2.4%	References 2, 5, 6, 7
Gastric	52 years	5%–7%	0.9%	References 2, 5, 8
Small bowel	47 years	0.4%–11%	0.3%	References 1, 5
Pancreas	No data	6.2%	1.6%	Reference 2
Biliary tract	50 years	1.9%–3.7%	0.2%	References 1, 2
Prostate	63 years	4.4%–13.8%	11.6%	See footnote h Reference 6
Breast (female)	No data	10.6%–18.6%	12.8%	See footnote i References 5, 9, 10, 11
Brain	No data	0.7%–1.7%	0.6%	References 6, 12
Skin	See footnote j References 13, 14			

Table 1. Cancer risks, genes associated and recommendations for management of hereditary CRC syndromes

Syndrome	Gene(s)	Lifetime cancer risks	% (95% CI)	Screening/surveillance	Preventative surgery
Lynch syndrome	MSH2 (10)	Colorectum	49 (29–85)	Colonoscopy every 1–2 years starting at age 20–25 years	Consider prophylactic hysterectomy once child bearing complete
		Endometrium	57 (22–82)	Consider upper endoscopy every 3–5 years, starting at age 30–35 years	
		Stomach	11–19	Consider endometrial cancer screening	
		Ovary	20 (1–66)		
		Hepatobiliary	2–7		
		Upper urinary tract	4–5		
		Pancreas	3–4		
		Small bowel	1–4		
		CNS (glioblastoma)	1–3		
	MLH1(10)	Colorectum	52 (31–90)	Colonoscopy every 1–2 years starting at age 20–25 years	Consider prophylactic hysterectomy once child bearing complete
		Endometrium	21 (9–82)	Consider upper endoscopy every 3–5 years, starting at age 30–35 years	
		Stomach	11–19	Consider endometrial cancer screening	
		Ovary	38 (3–81)		
		Hepatobiliary	2–7		
		Upper urinary tract	4–5		
		Pancreas	3–4		
		Small bowel	1–4		
		CNS (glioblastoma)	1–3		

Pembrolizumab in MMRD CRC: Duration of Disease Control

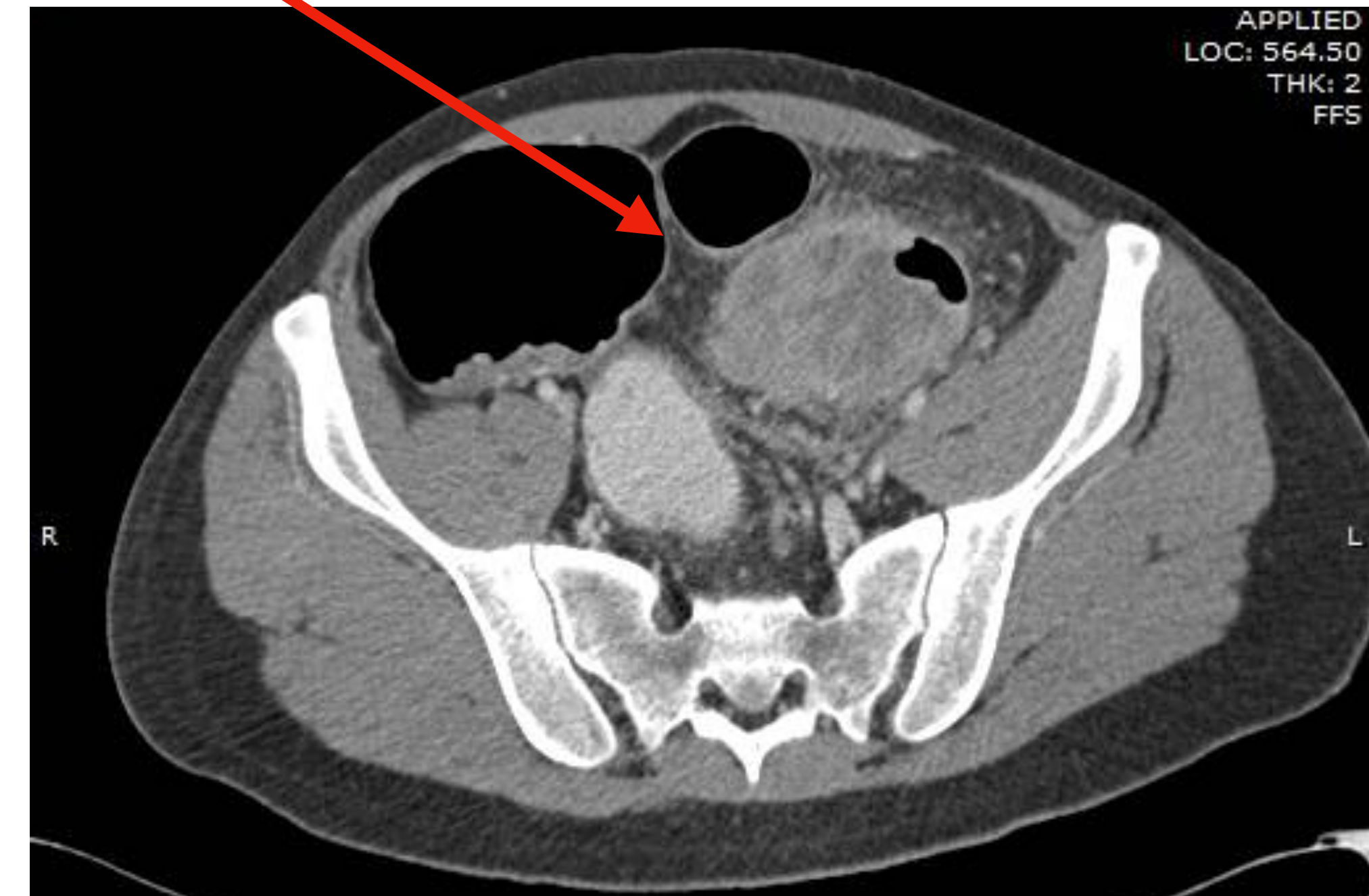
- Complete and durable responses observed in > 50% of pts with MMRD CRC



32-year old male

Sigmoid mass

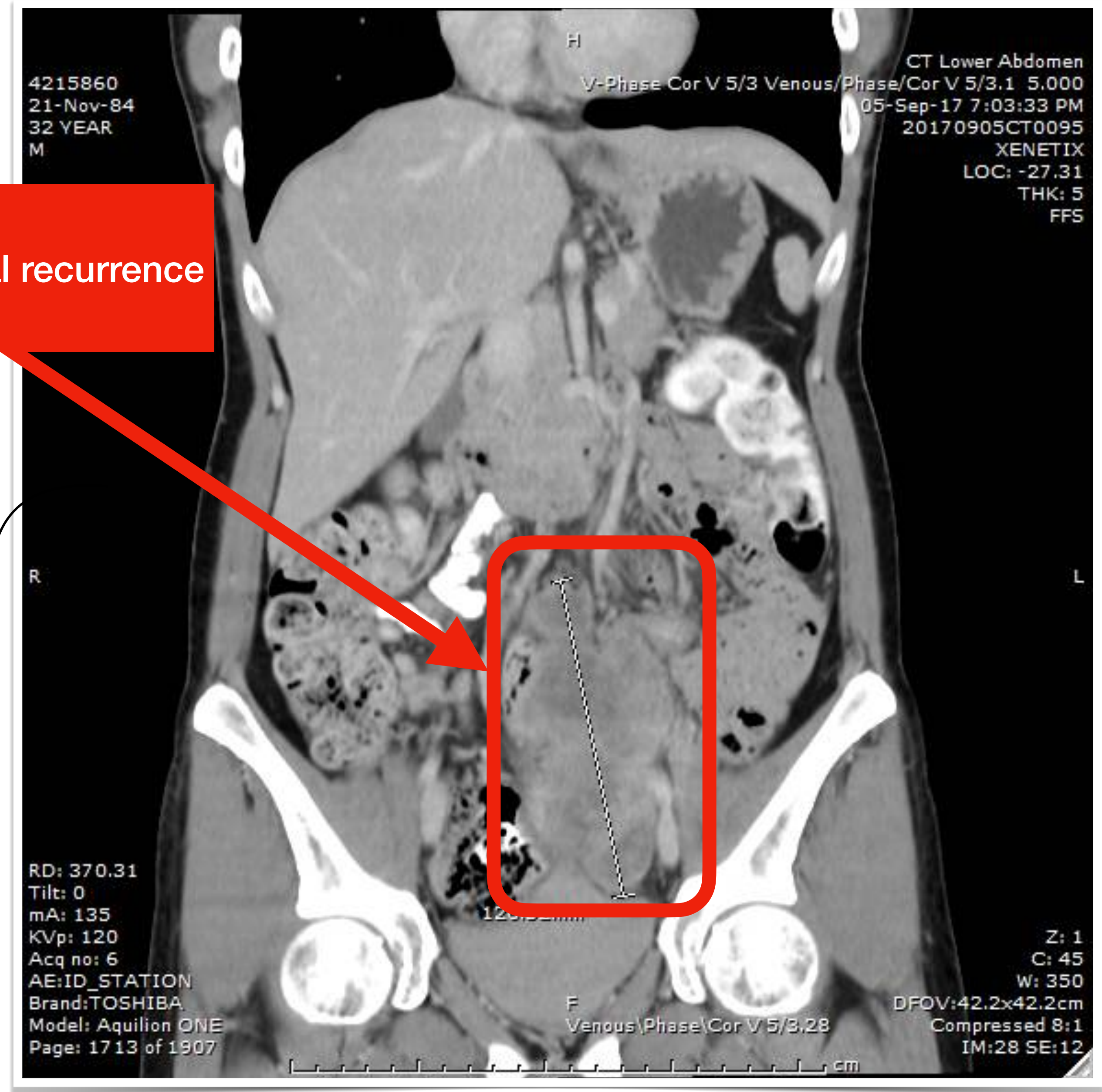
- 32 year-old gentleman
No underlying disease
His uncle has colonic cancer at 40 years old
- Presented with lower GI bleeding for 1 month
- Colonoscopy findings:
 - Circumferential mass with contact bleeding at sigmoid colon , incomplete colonoscopy due to obstruction



Post Sx for 3 months

12 cm local recurrence

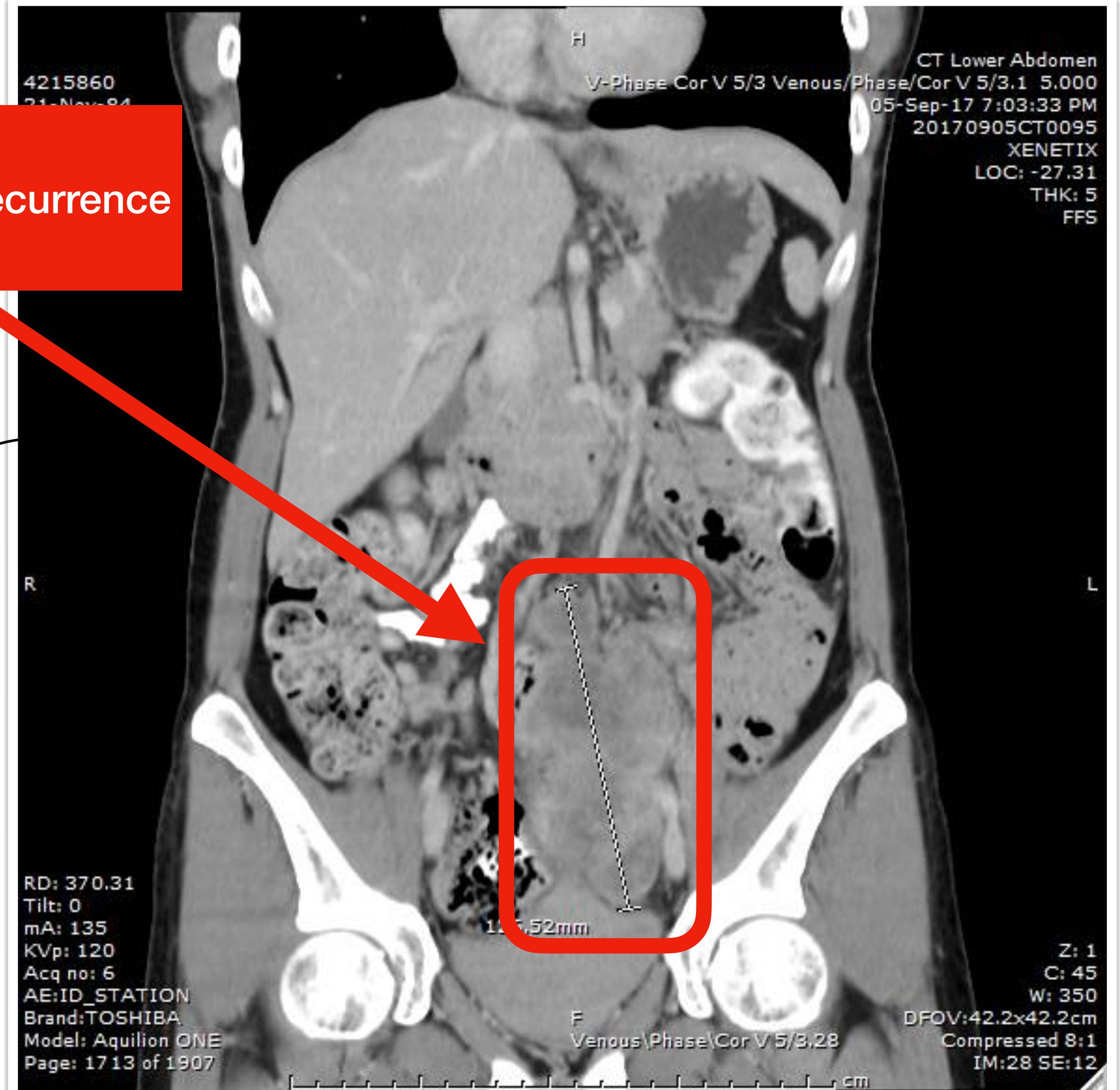
- F/U CT whole abdomen findings:
 - A 12 cm mass at distal descending colon with encasement of left mid-ureter
 - Intraabdominal LN 0.6 cm
- Colonoscopy finding :
 - Rectosigmoid mass 15 cm from AV
 - Can't pass scope



Post Sx for 3 months

12 cm local recurrence

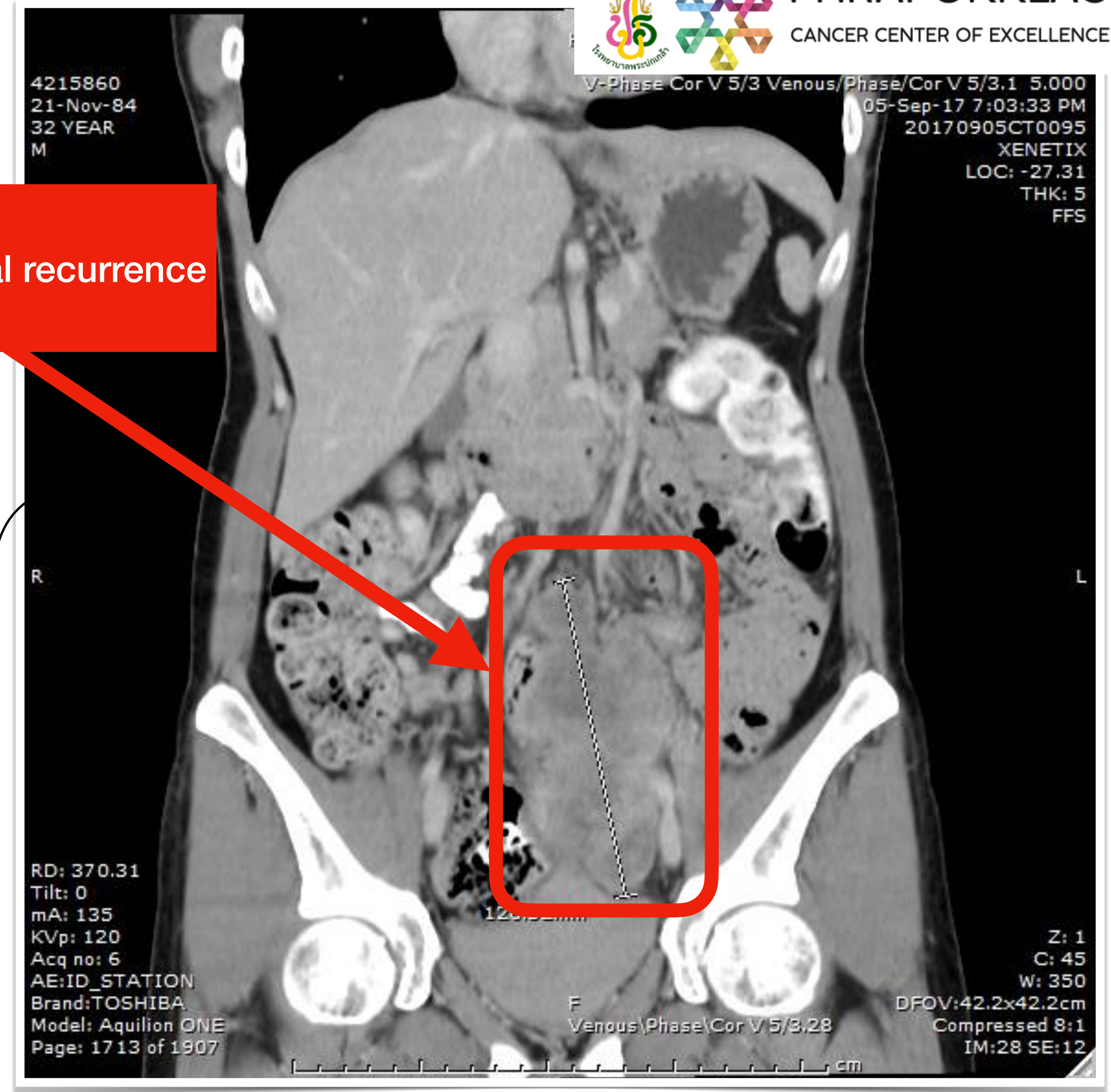
- Rx : Preop plan total colectomy
But intraoperative findings : multiple mesenteric LNs
- What is the next management?



Post Sx for 3 months

12 cm local recurrence

- Rx : 1L FOLFOXIRI

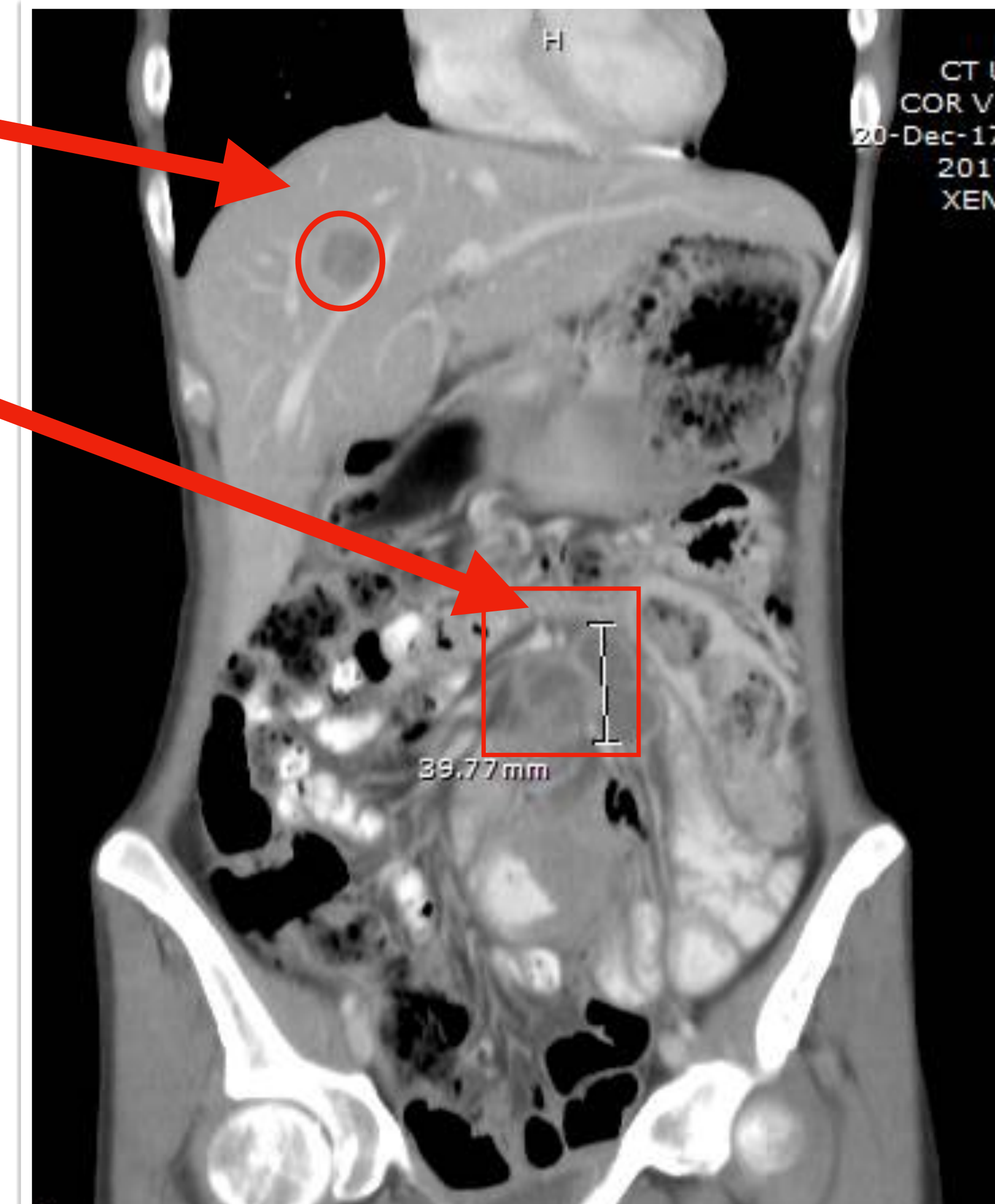


Post 4 cycles of FOLFOXIRI

- Clinical : pain at mid abdomen refer to back
and need for MST (10) 1 tab po bid
and rescue MIR (10) 1 tab/Day
- CT Whole abdomen **PD** at
 - increased size recurrent tumor **7.8 > 18.3 cm**
 - increased size intraabdominal matted **LN 2.9 cm**
 - new hepatic metastasis size 2.3 cm at S8**
- What is your next management?

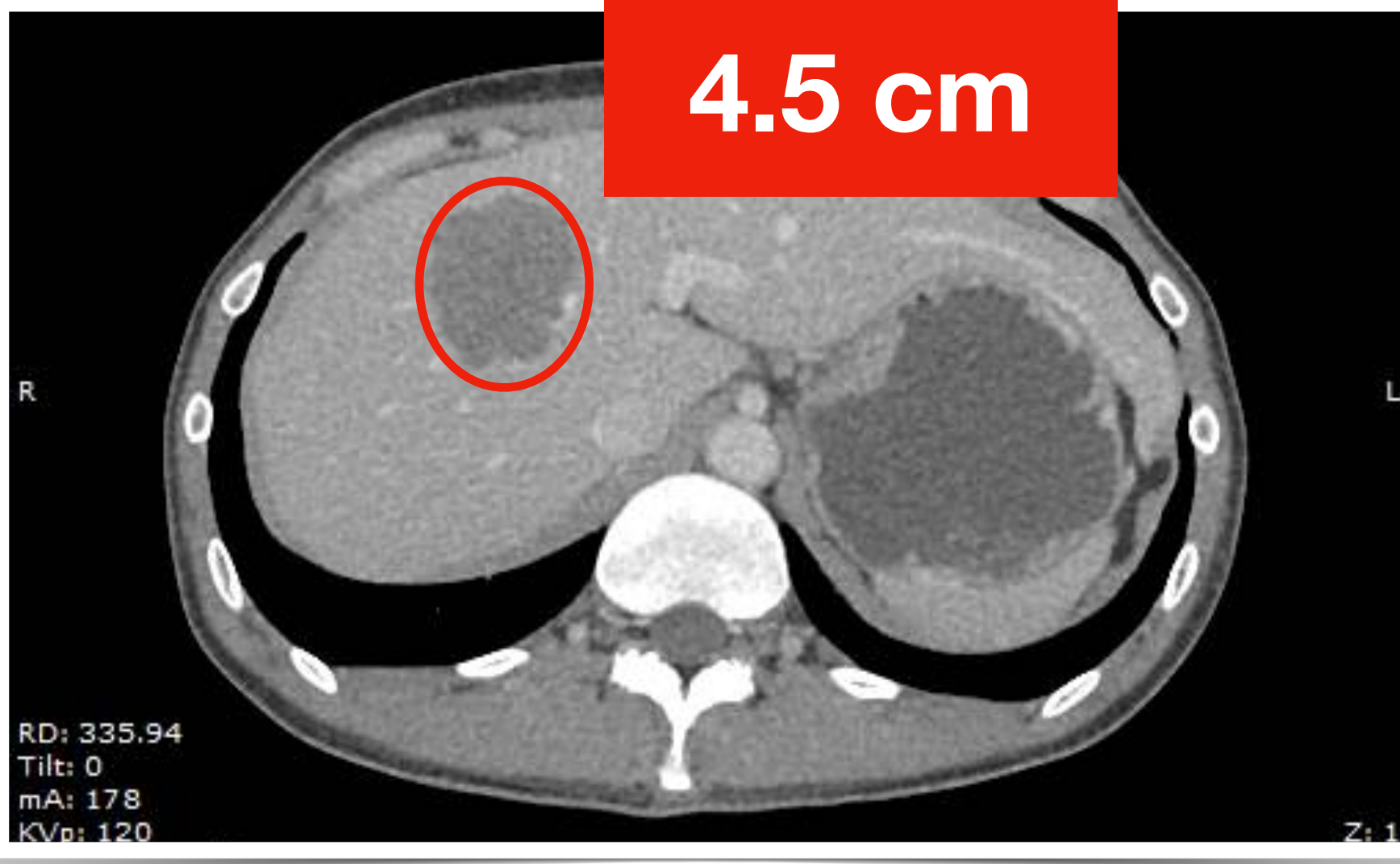
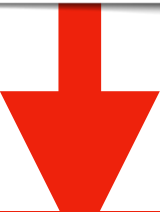
New liver
metastasis

Increased size
& Matted LN



Progression Note

pembrolizumab cycles	Baseline	post RT at sigmoid & IMV and post C4
Sigmoid site (Thickness x lenght) (cm)	1.8 x 18	1.8 x <u>13</u>
IMV LN (cm)	3.9	<u>2.6</u> (Decreased 33%)
Liver metastasis (cm)	2.3	<u>4.5</u> (increased 95%)
CEA	-	2.18



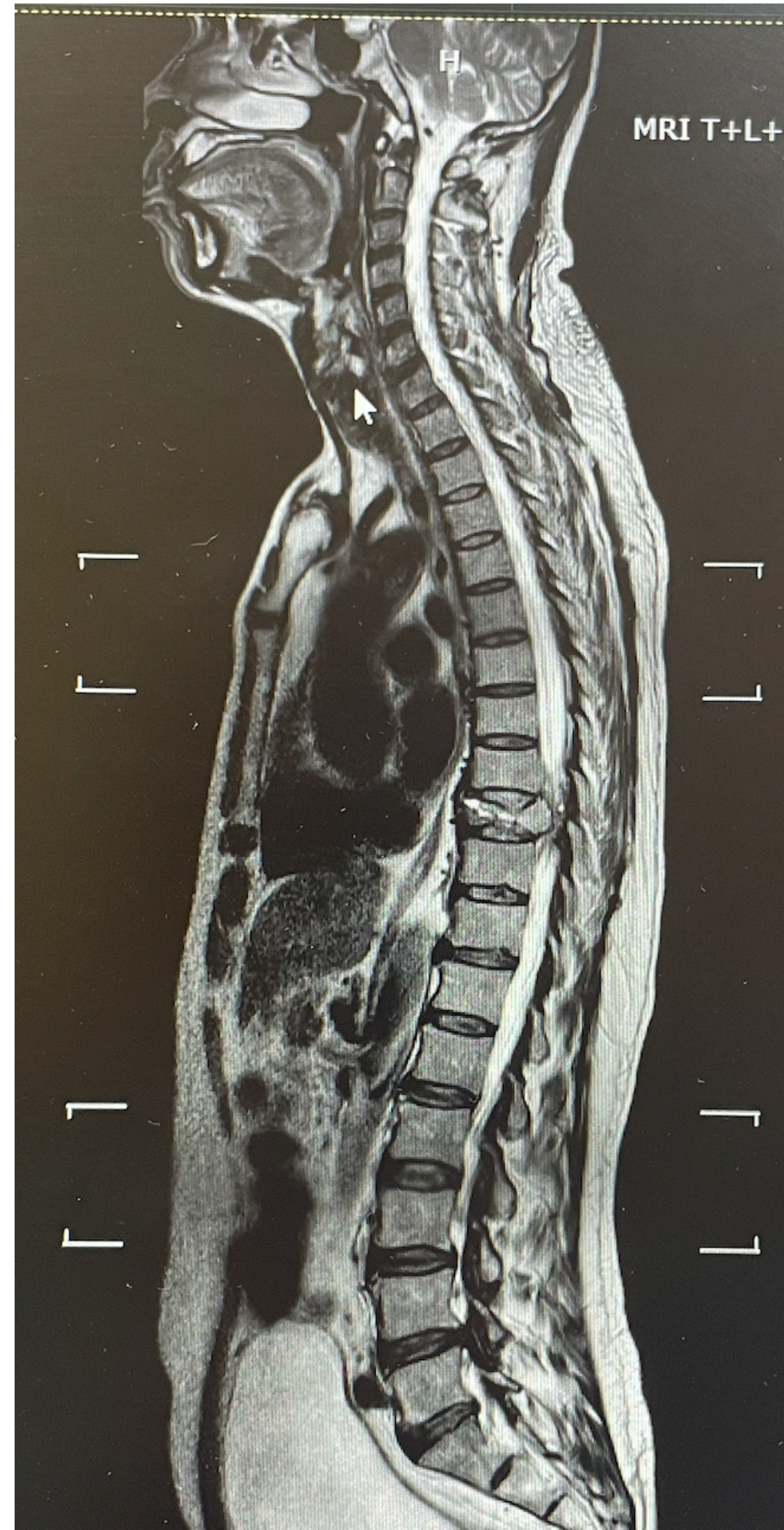
Progression Note

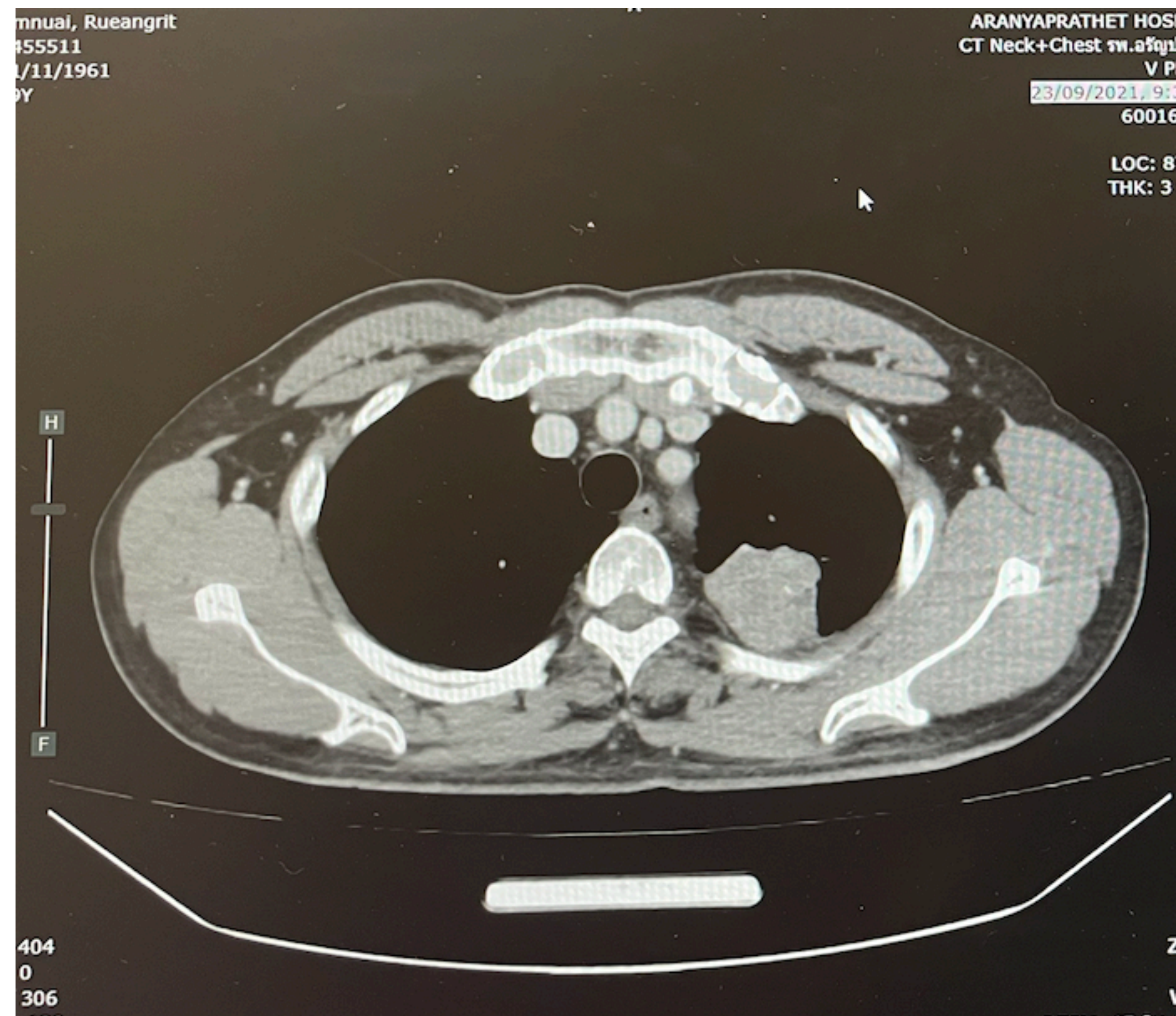
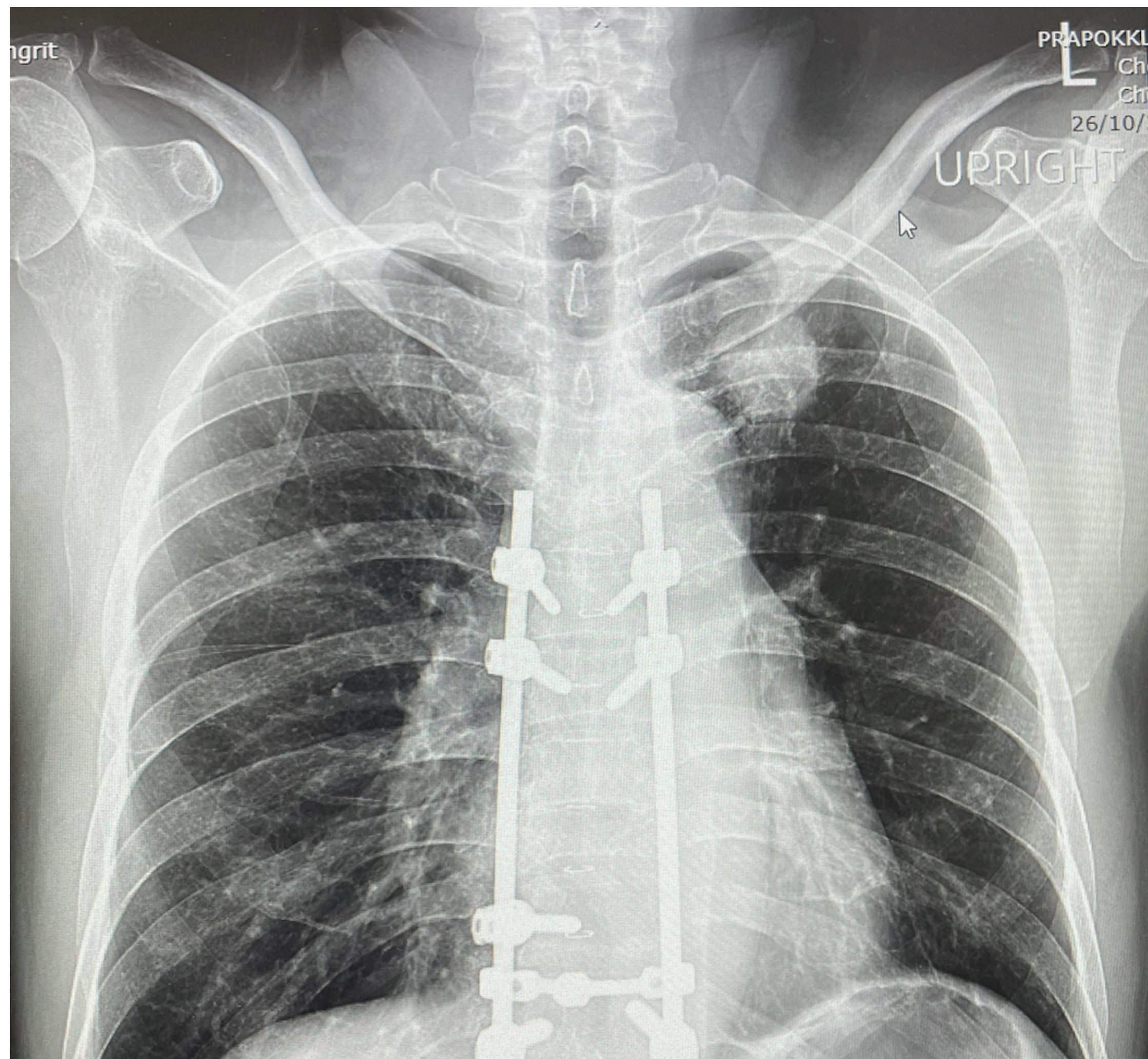
pembrolizumab cycles	Baseline	post RT at sigmoid & IMV and post C4	post C6	post C13	post C18 then Stop IO	after stop for 3 mos	after stop for 8 mos	after stop for 11 mos
Sigmoid site (Thickness x lenght) (cm)	1.8 x 18	1.8 x <u>13</u>	<u>0.8</u> x 13	stable size				
IMV LN (cm)	3.9	<u>2.6</u> (Decreased 33%)	<u>2.3</u> (Sum Decreased 41%)	stable size				
Liver metastasis (cm)	2.3	<u>4.5</u> (increased 95%)	<u>4.5</u> (stable size)	stable size				
CEA		2.18	1.08	-	-	1.28	1.05	0.88

case sharing

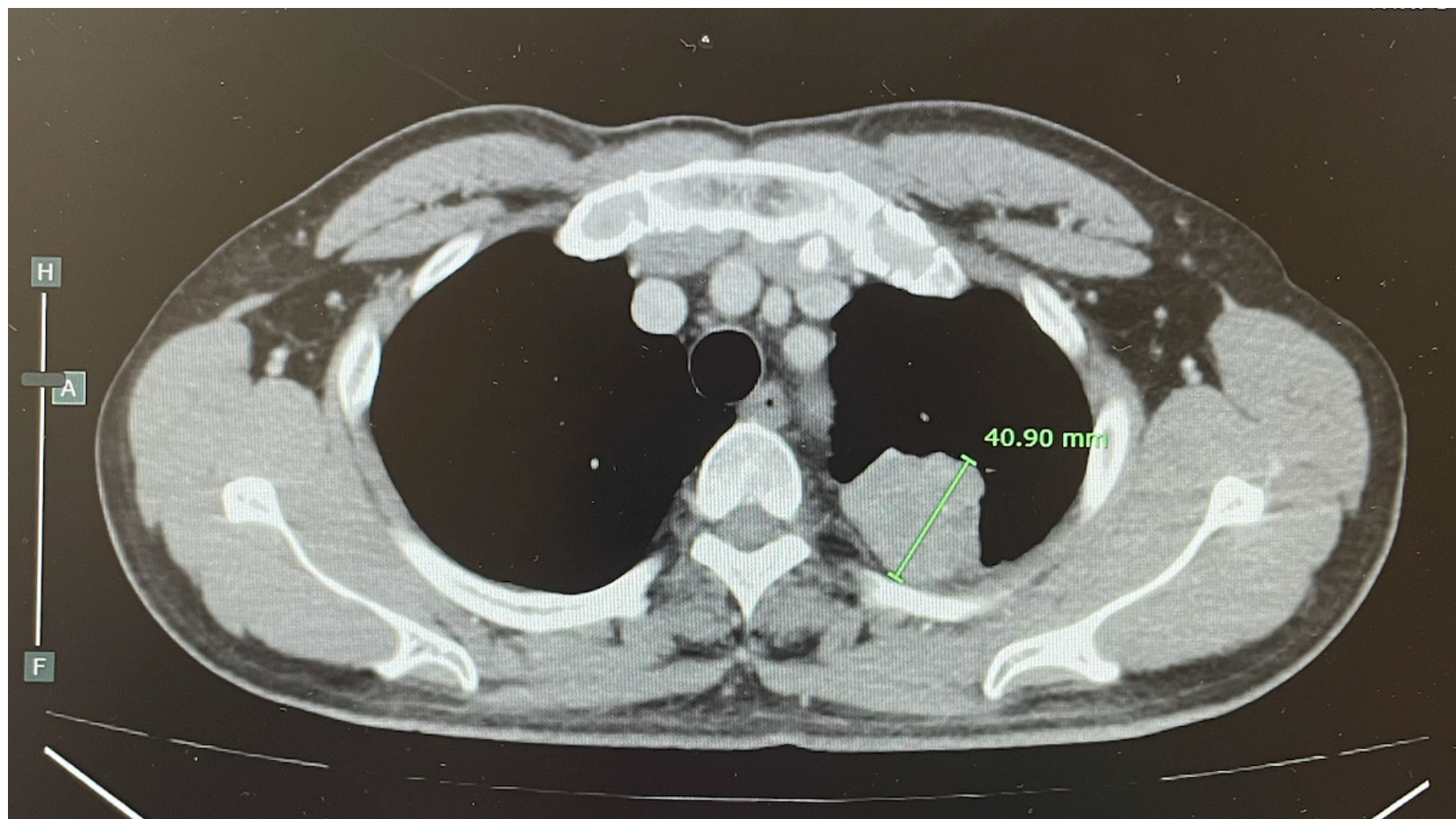
59 Year old Gentleman

- Presented c backache
- Ortho consultation :
unstable spinal
metastasis with cord
compression T9
- Post ORIF T6-12 c
decompression T9
- Patho : metastasis
ADC , mod diff

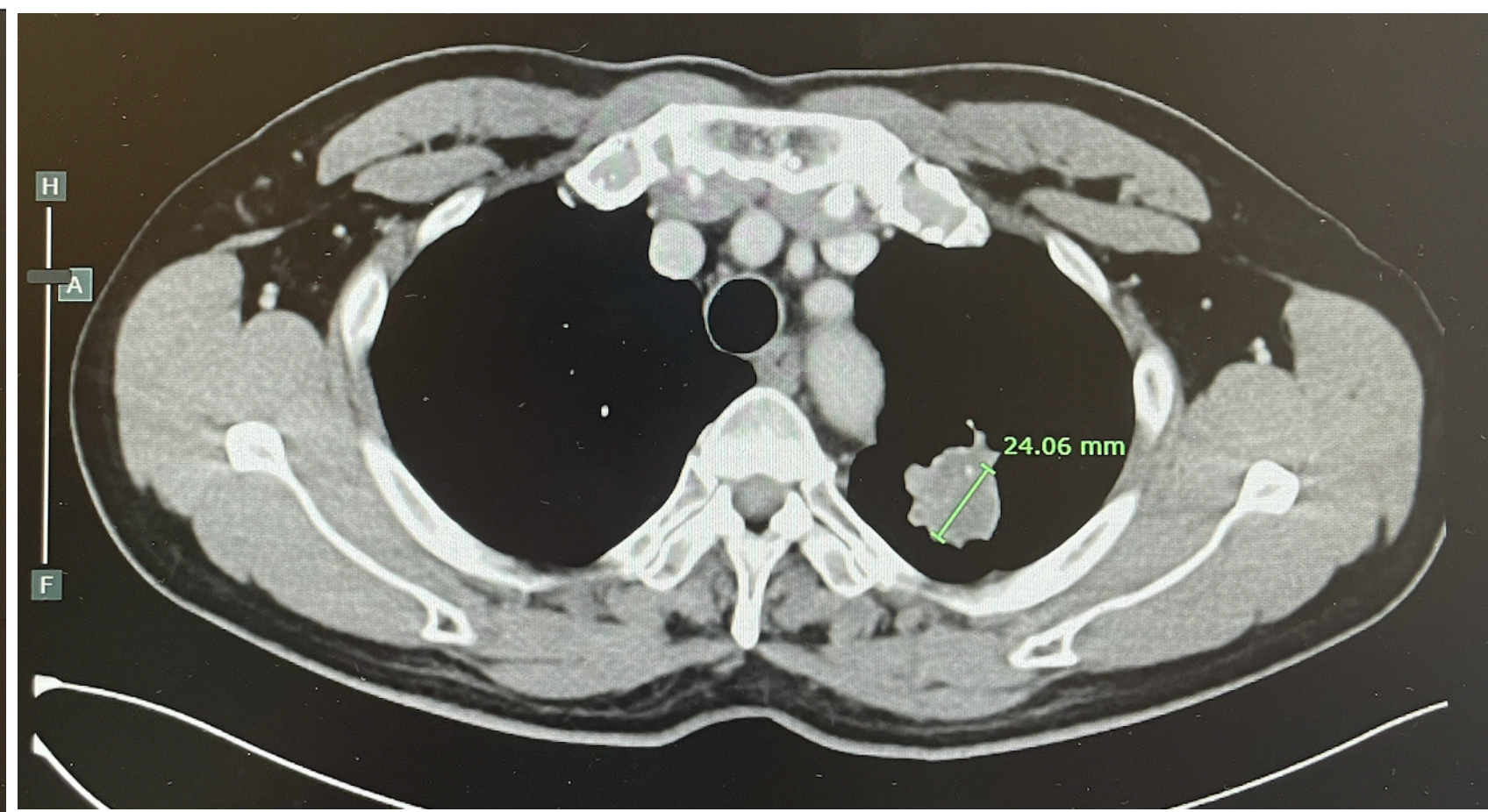




- Tissue EGFR = Exon 19 deletion
- Start erlotinib since 25/10/64



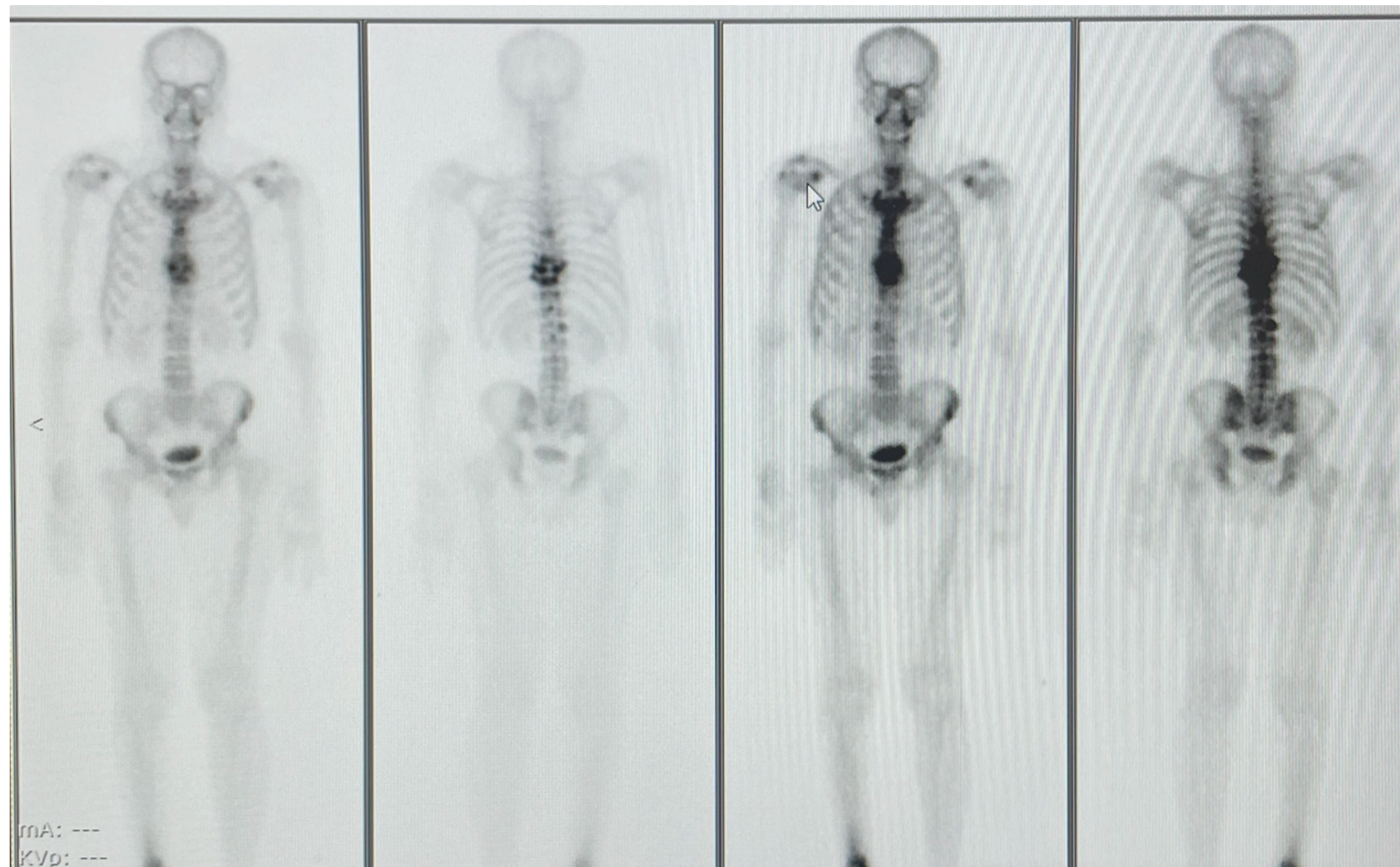
23/9/64
Baseline



28/2/66

PR

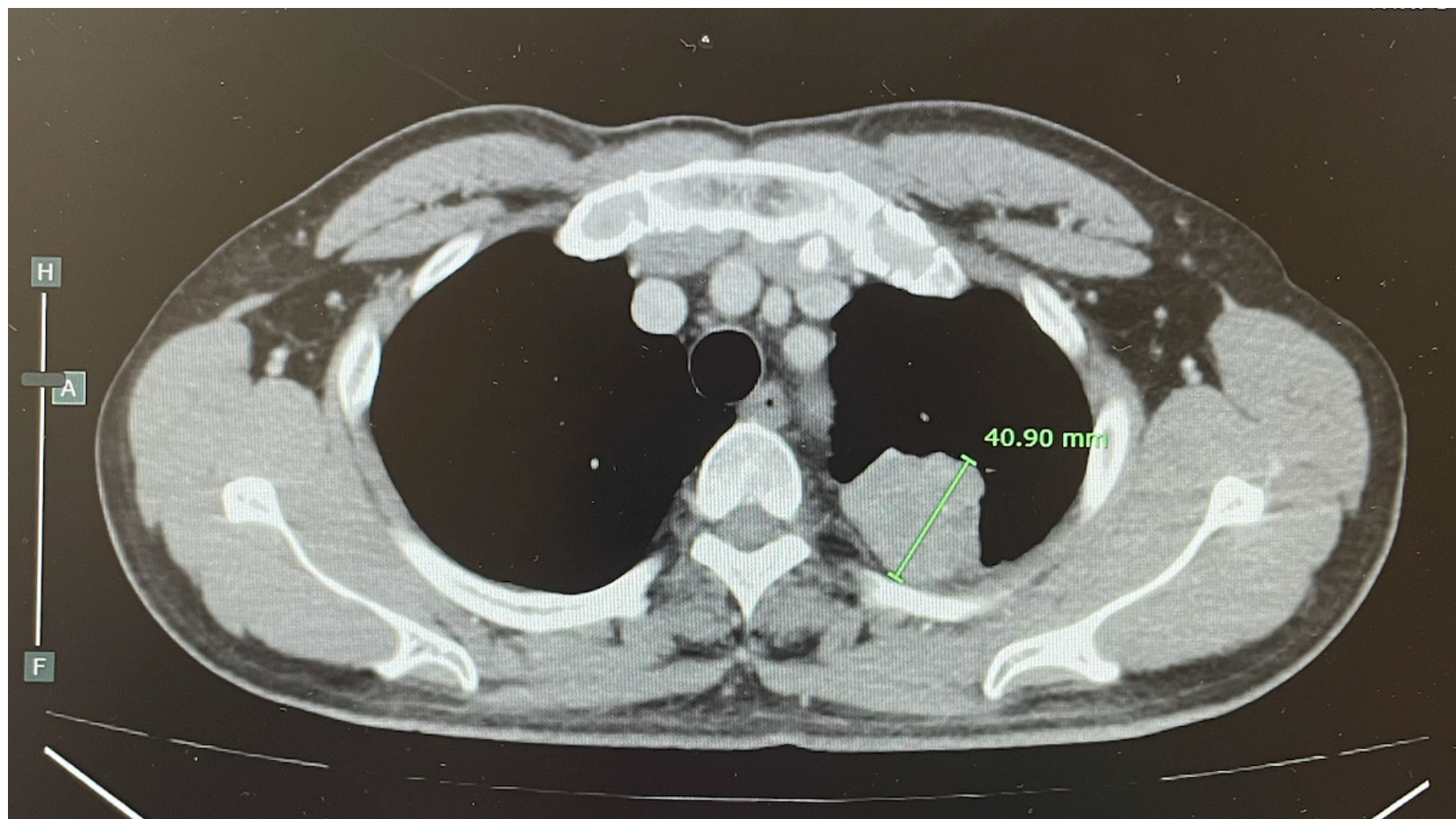
19/11/64



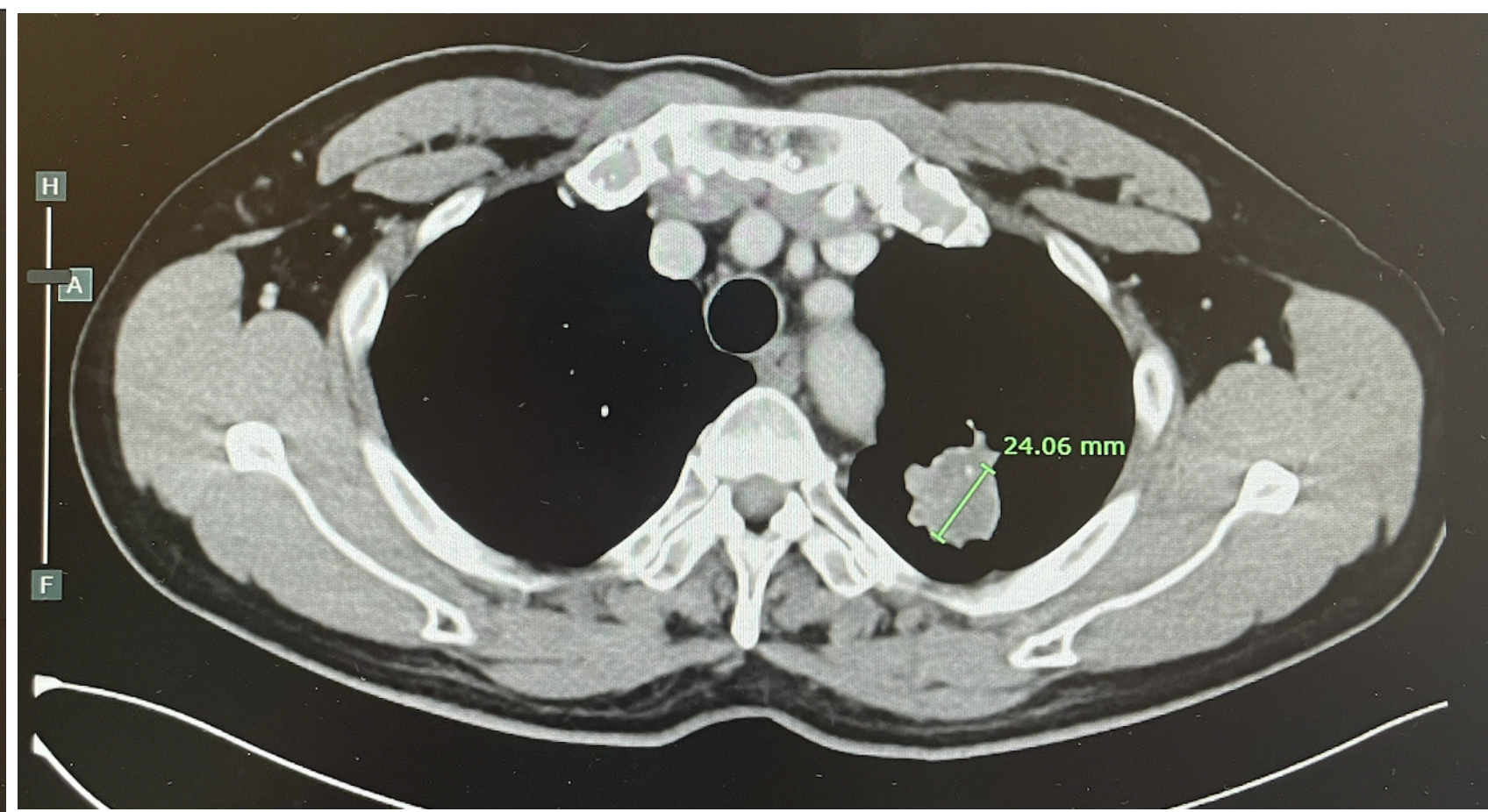
19/6/66



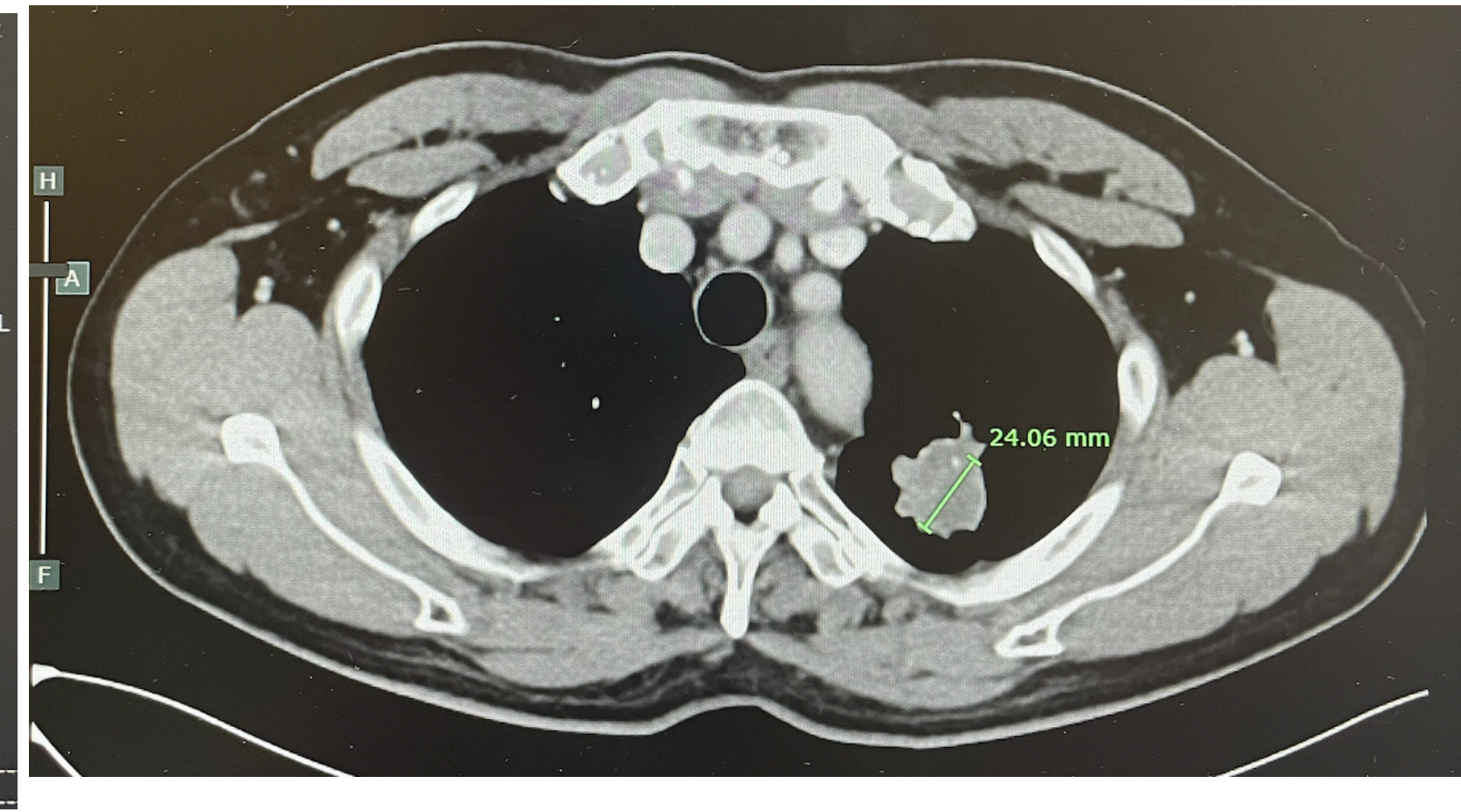
- Tissue EGFR = L858R Mutation
- Start erlotinib since 25/10/64



23/9/64
Baseline

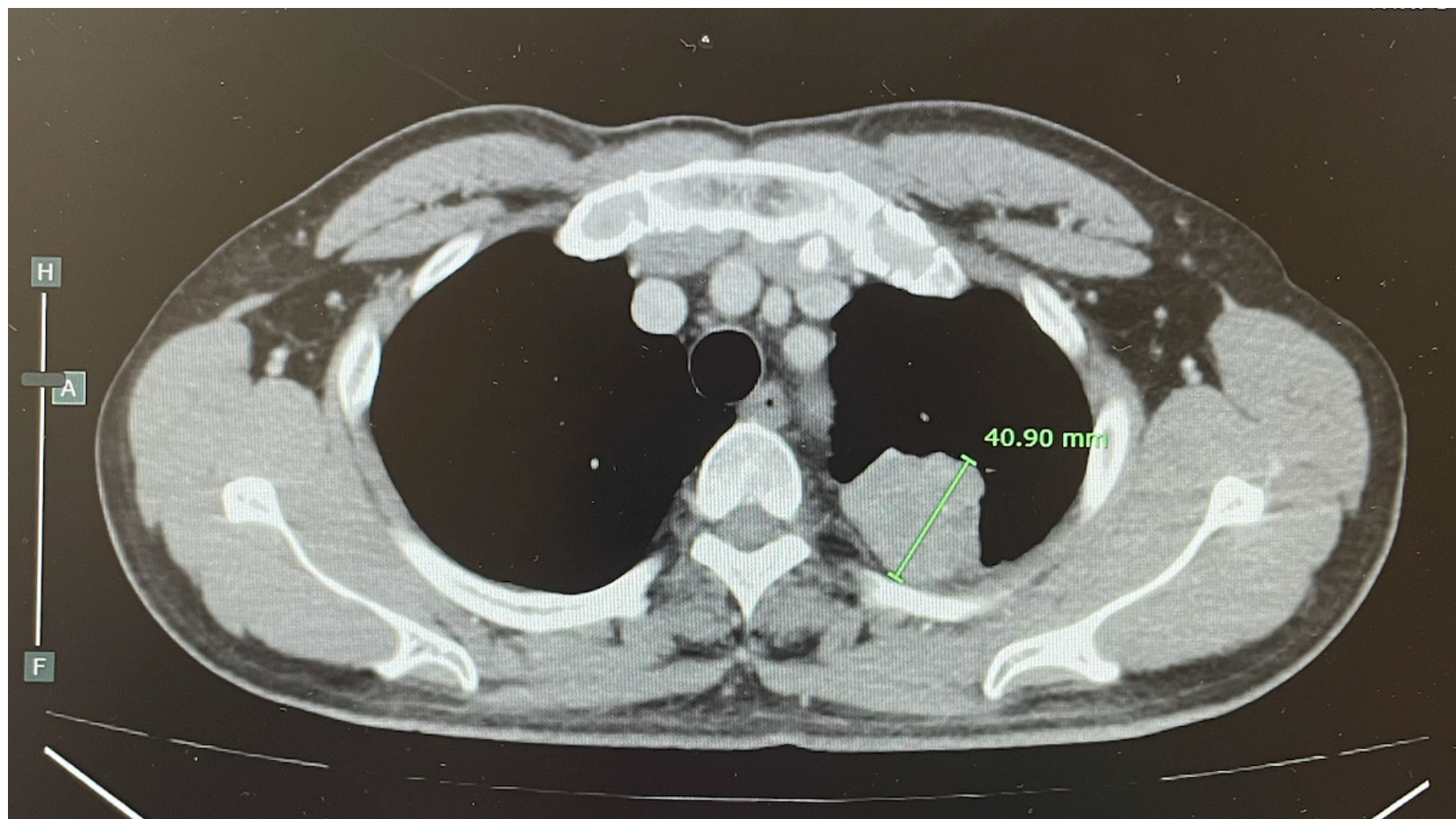


28/2/66
PR

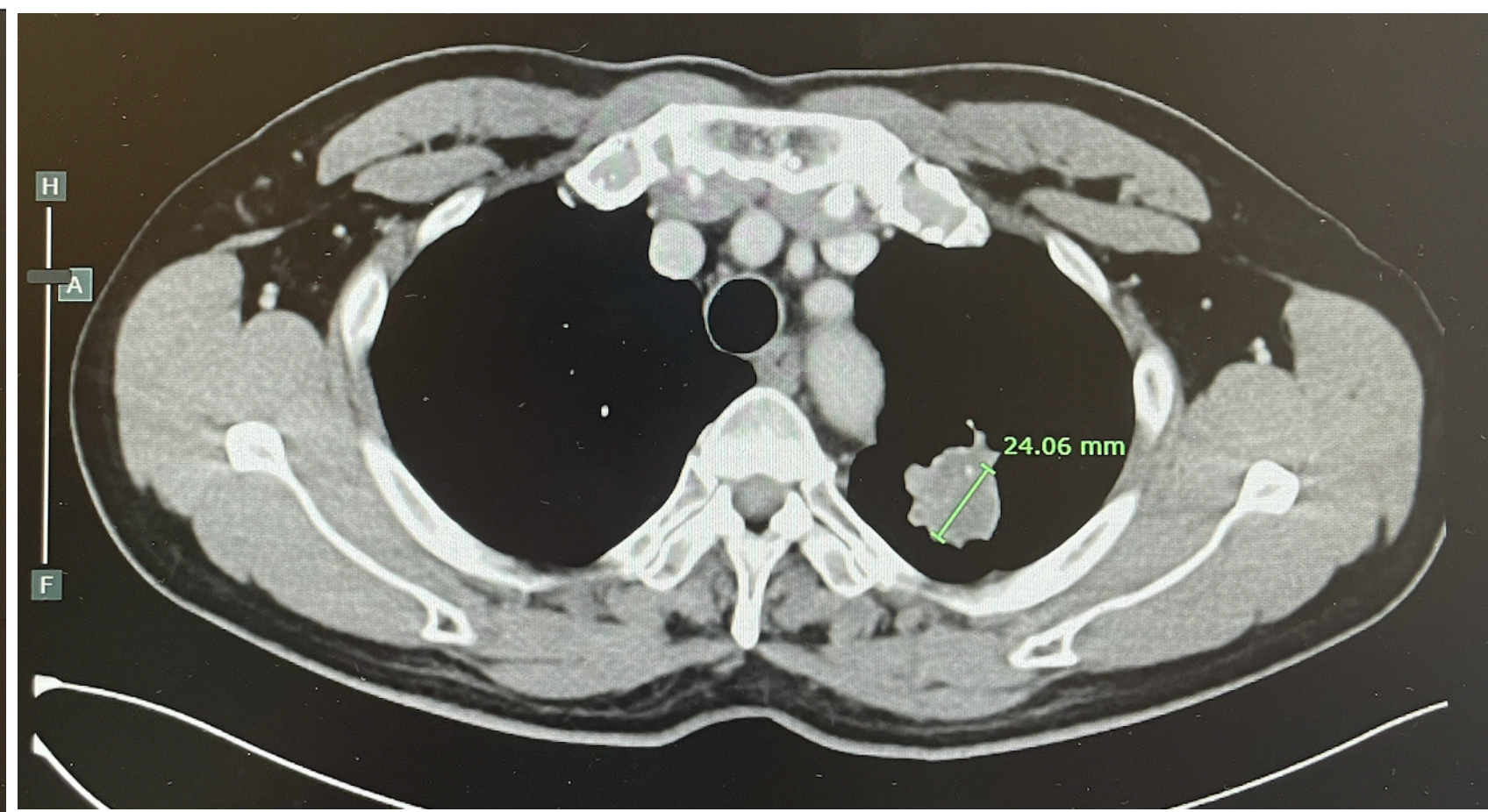


24/5/66
PD

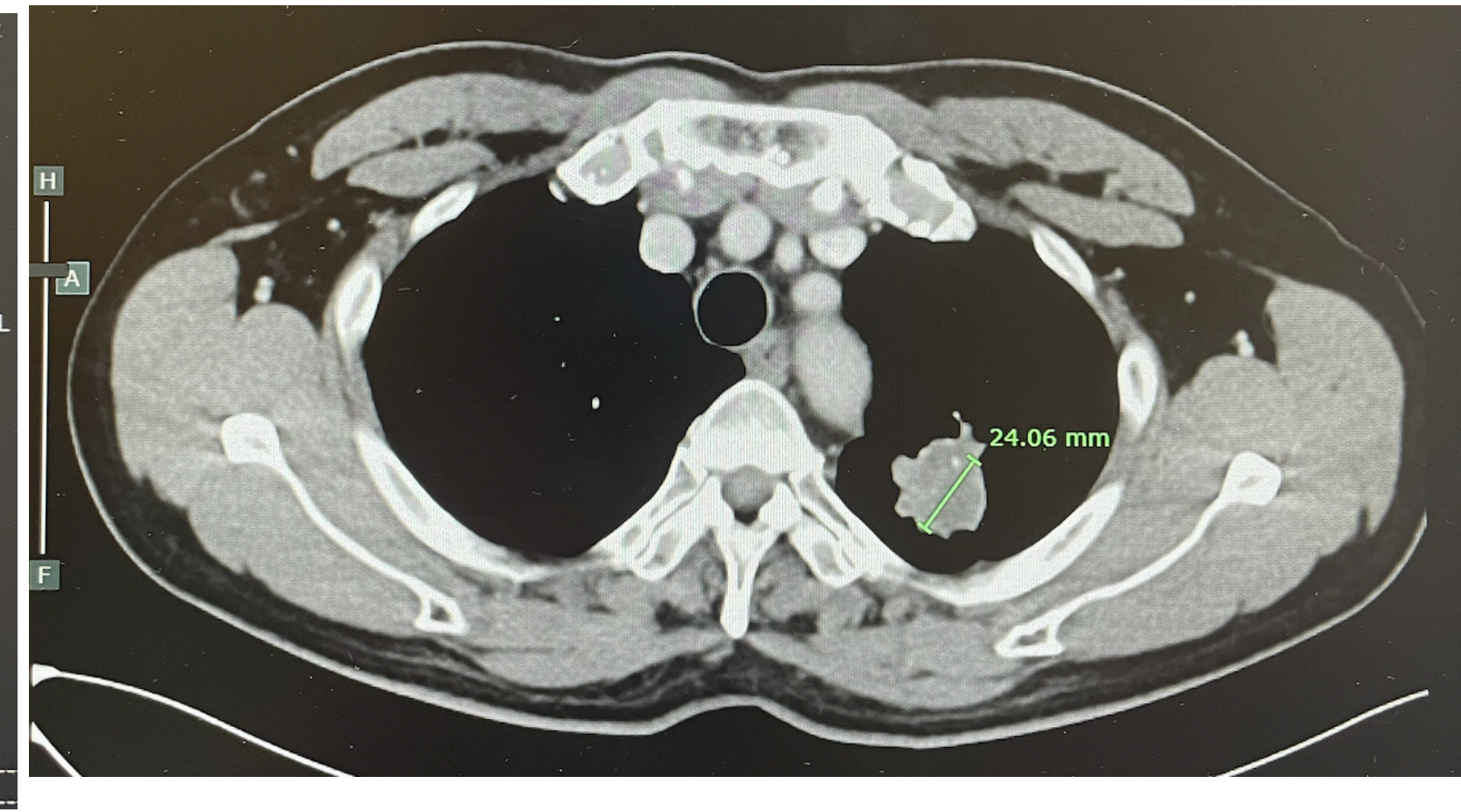
- Tissue EGFR = L858R Mutation
- Start erlotinib since 25/10/64



23/9/64
Baseline



28/2/66
PR



24/5/66
PD

- Then Cb/gem > docetaxel
- Then PD
- Then send Plasma EGFR



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 Email: ppkgenomiclab@gmail.com


 6455511

 23121370228

GENOMIC LABORATORY REPORT

Patient Name : นายชำนาญ เรืองฤทธิ์ [ชาย] 62 ปี	Lab No. : 23121370228
Hospital No. : 6455511	Sex : Male
Order Date : 13 Dec 2023	Age : 62 Y
Received Date : 13 Dec 2023	DOB : 01 Nov 1961
Diagnosis : Lung Cancer	Received Tissue : N/A
	Doctor : นพ. ศาสกร วันชัยจิระบุญ

Test Name	Result	Reference Range
EGFR mutation (Plasma) :	Mutation Detected : Ex19Del, T790M	<i>Mutation Detected: Mutation detected in specified targeted EGFR region</i> <i>No Mutation Detected: Mutation not detected in targeted EGFR region</i>

Ex19Del , T790M

Method and Coverage

EGFR mutation test was performed, using the FDA-approved Cobas EGFR Mutation Test V.2 (Roche Molecular System, Inc.)

The Cobas EGFR Mutation Test V.2 using allele specific PCR technology to detect the following mutation

Exon 18 : G719X (G719A, G719C, and G719S)

Exon 19 : Deletion and complex mutations

Exon 20 : S768I, T790M, and insertions

Exon 21 : L858R and L861Q

Limit of Detection : 5% mutant alleles in tissue, and 100 copies/ml mutant DNA in plasma

Pathological Review

Pathological review of the tissue section before molecular analysis

Block No. : N/A

Tumor area was reviewed and selected by pathologist

Amount of malignant cells available for EGFR mutation testing : N/A

Reviewed Date : N/A

Pathologist : N/A

- Then Cb/gem > docetaxel
- Then PD
- Then send Plasma EGFR
- Then TS-1



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 Chanthaburi 22000, Thailand
 Tel. +66 39 319 666 : 8241, 8242
 Email: ppkgenomiclab@gmail.com


 6455511

 23121370228

GENOMIC LABORATORY REPORT

Patient Name : นายชำนาญ เรืองฤทธิ์ [ชาย] 62 ปี	Lab No. : 23121370228
Hospital No. : 6455511	Sex : Male
Order Date : 13 Dec 2023	Age : 62 Y
Received Date : 13 Dec 2023	DOB : 01 Nov 1961
Diagnosis : Lung Cancer	Received Tissue : N/A
	Doctor : นพ. ศาสกร วันชัยจิระบุญ

Test Name	Result	Reference Range
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Ex19Del , T790M

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Pathological Review

Pathological review of the tissue section before molecular analysis

Block No. : N/A

Tumor area was reviewed and selected by pathologist

Amount of malignant cells available for EGFR mutation testing : N/A

Reviewed Date : N/A

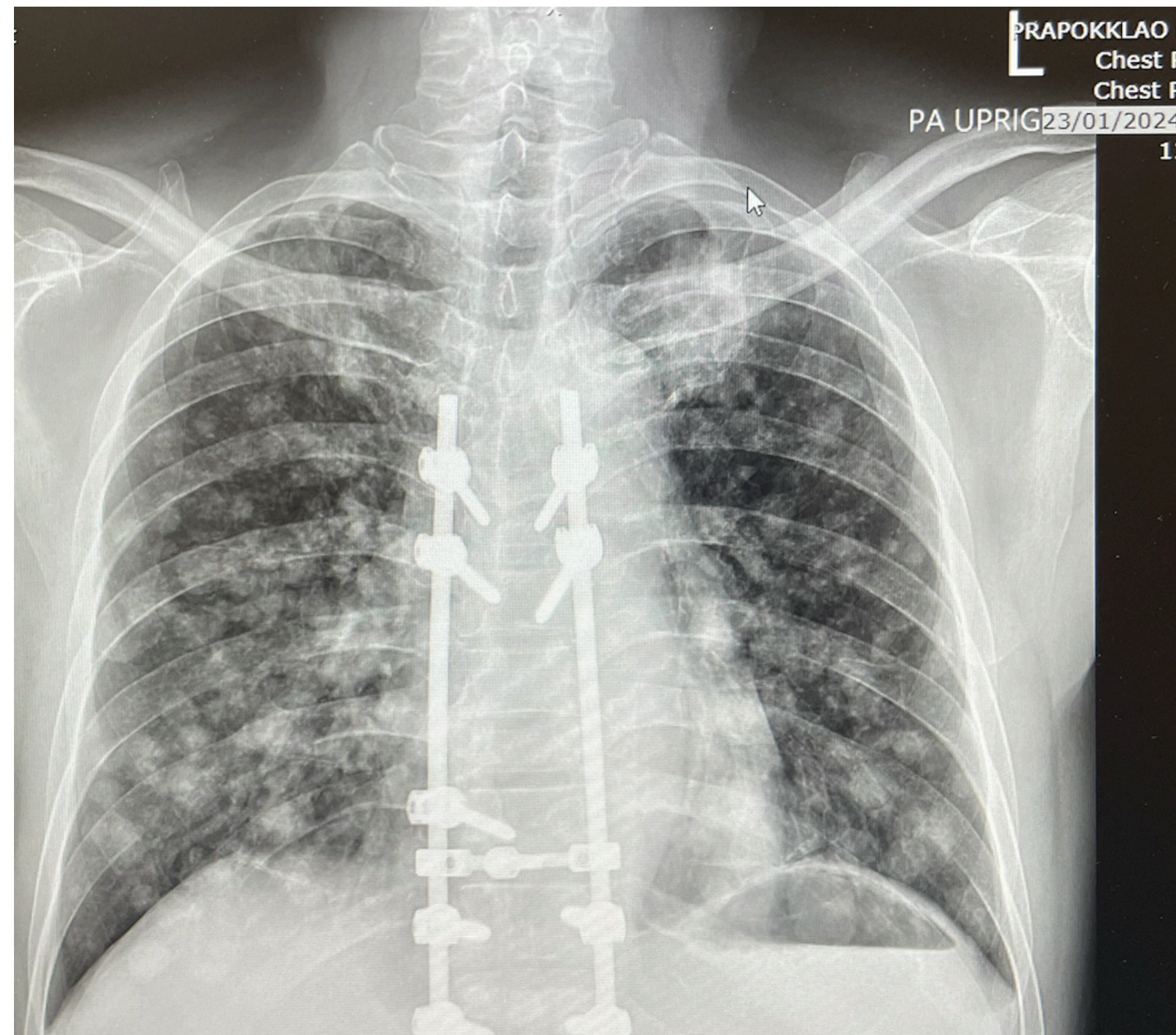
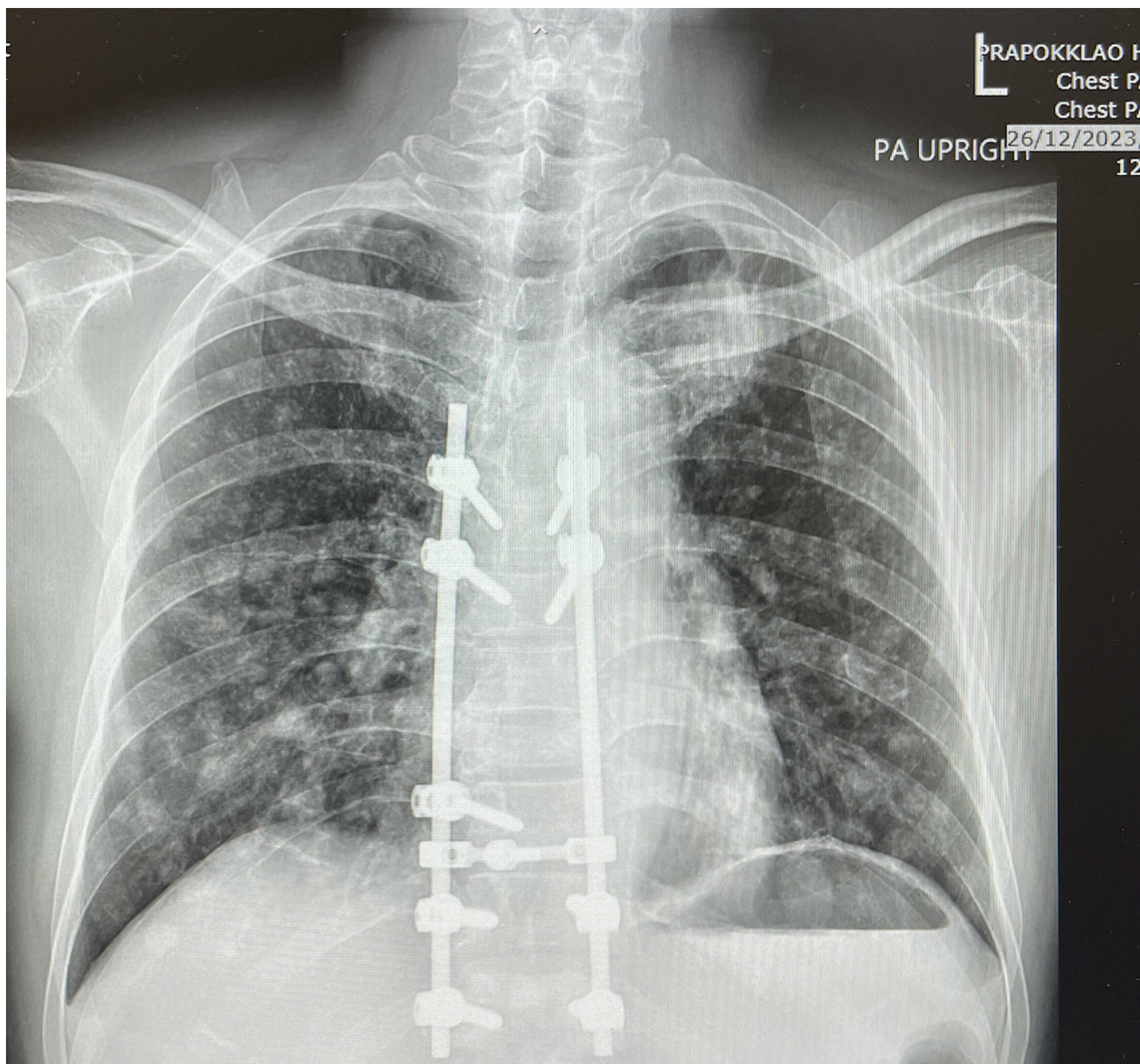
Pathologist : N/A

Baseline

26-12-66

TS-1 x1 course

23-1-67



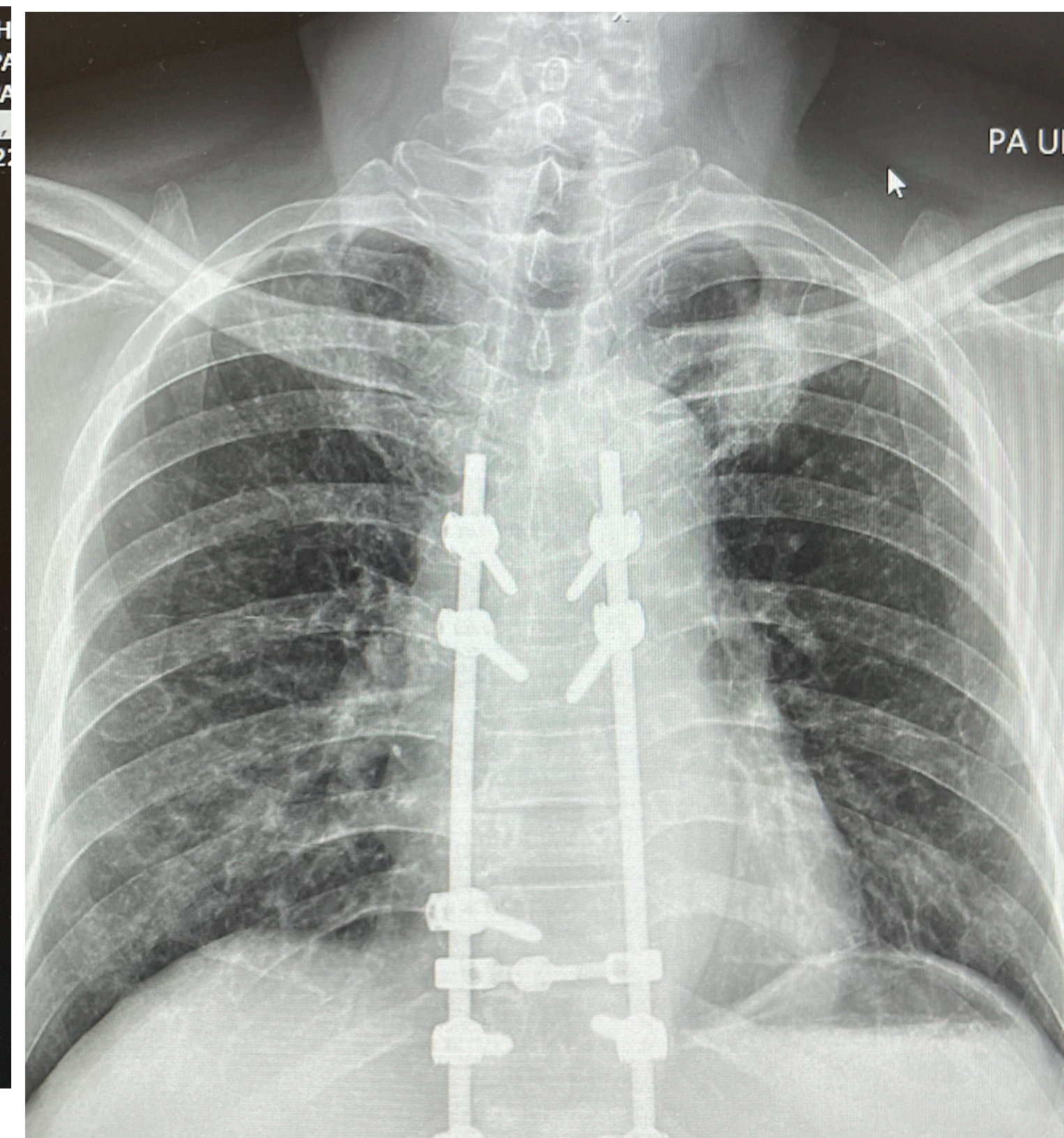
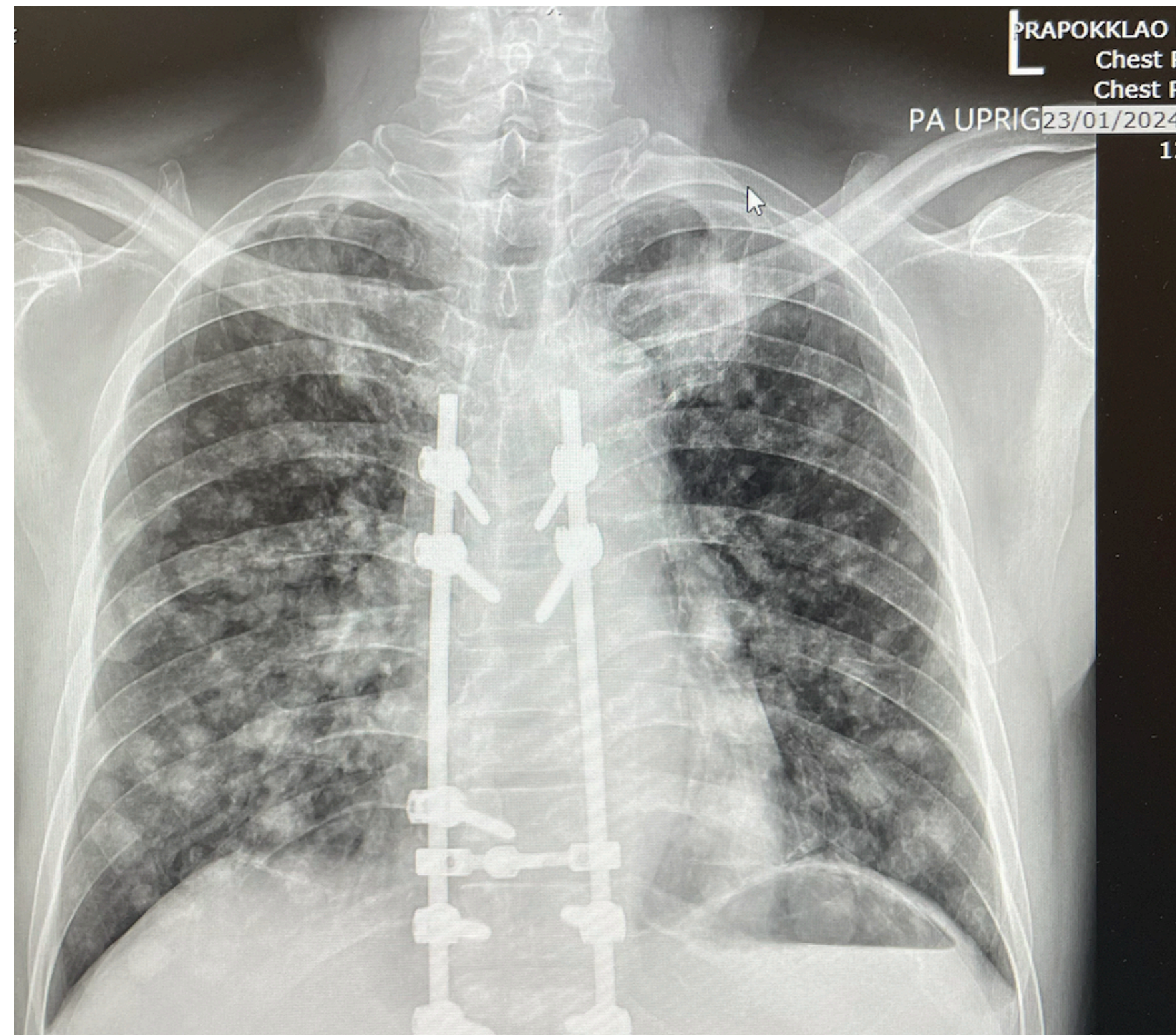
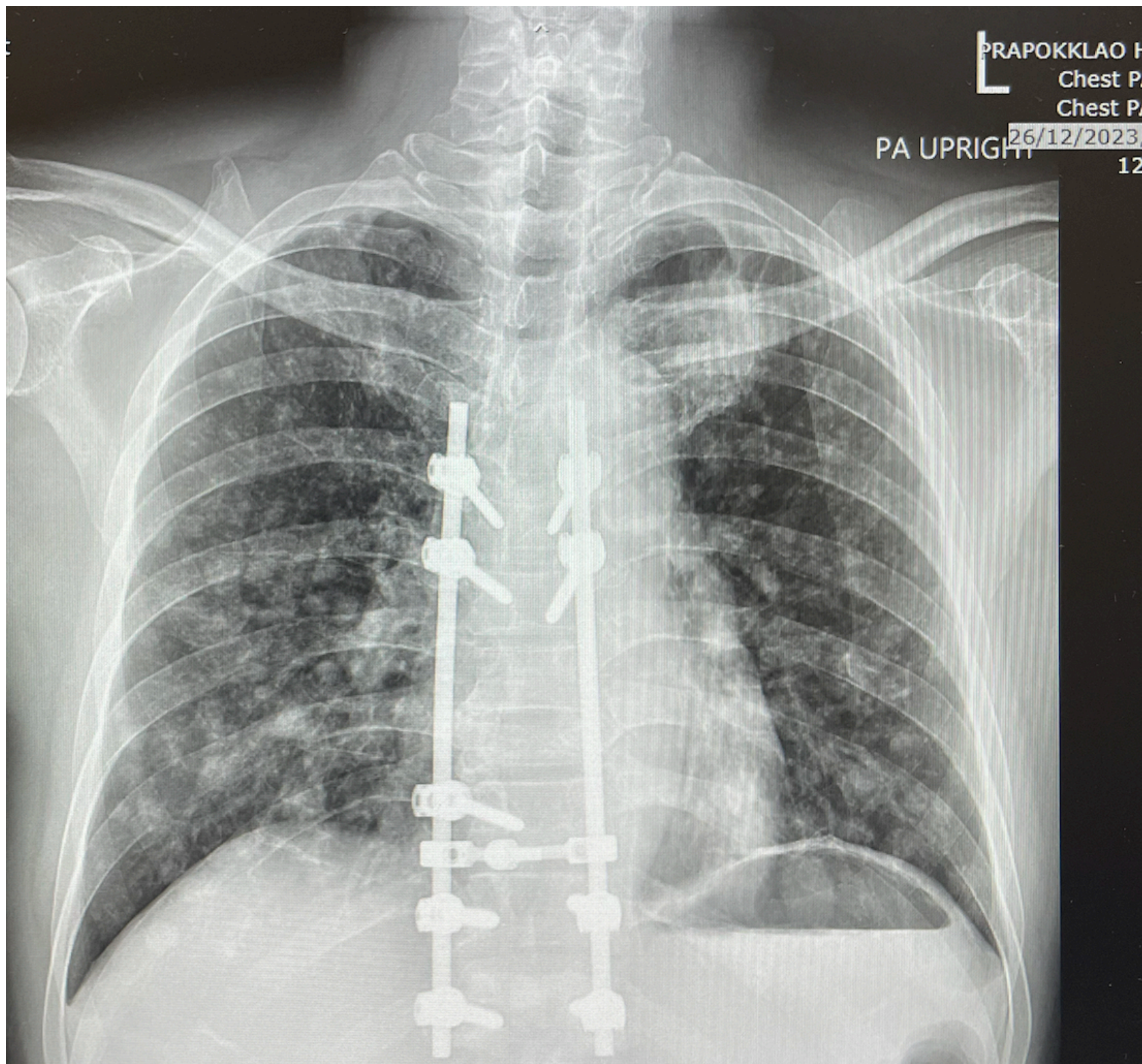
Baseline

26-12-66

23-1-67

2 weeks of Osimertinib

7-2-67



Test Name	Result	Reference Range
KRAS mutation	Mutation Detected : G12X	<i>Mutation Detected: Mutation detected in specified targeted KRAS region</i> <i>No Mutation Detected: Mutation not detected in targeted KRAS region</i>

X

A

C

D

R

S

V

Method and Coverage

KRAS mutation test was performed, using the KRAS Mutation Test V.2 (Roche Molecular System, Inc.)

The Cobas KRAS Mutation Test V.2 uses parallel specific PCR technology to detect the following 28 mutations.

Exon 2 : G12X (G12A, G12C, G12D, G12R, G12S, G12V)

G13X (G13A, G13C, G13D, G13R, G13S, G13V)

Exon 3 : A59X (A59E, A59G, A59S, A59T)

Q61X (Q61E, Q61Hc, Q61Ht, Q61K, Q61L, Q61P, Q61R)

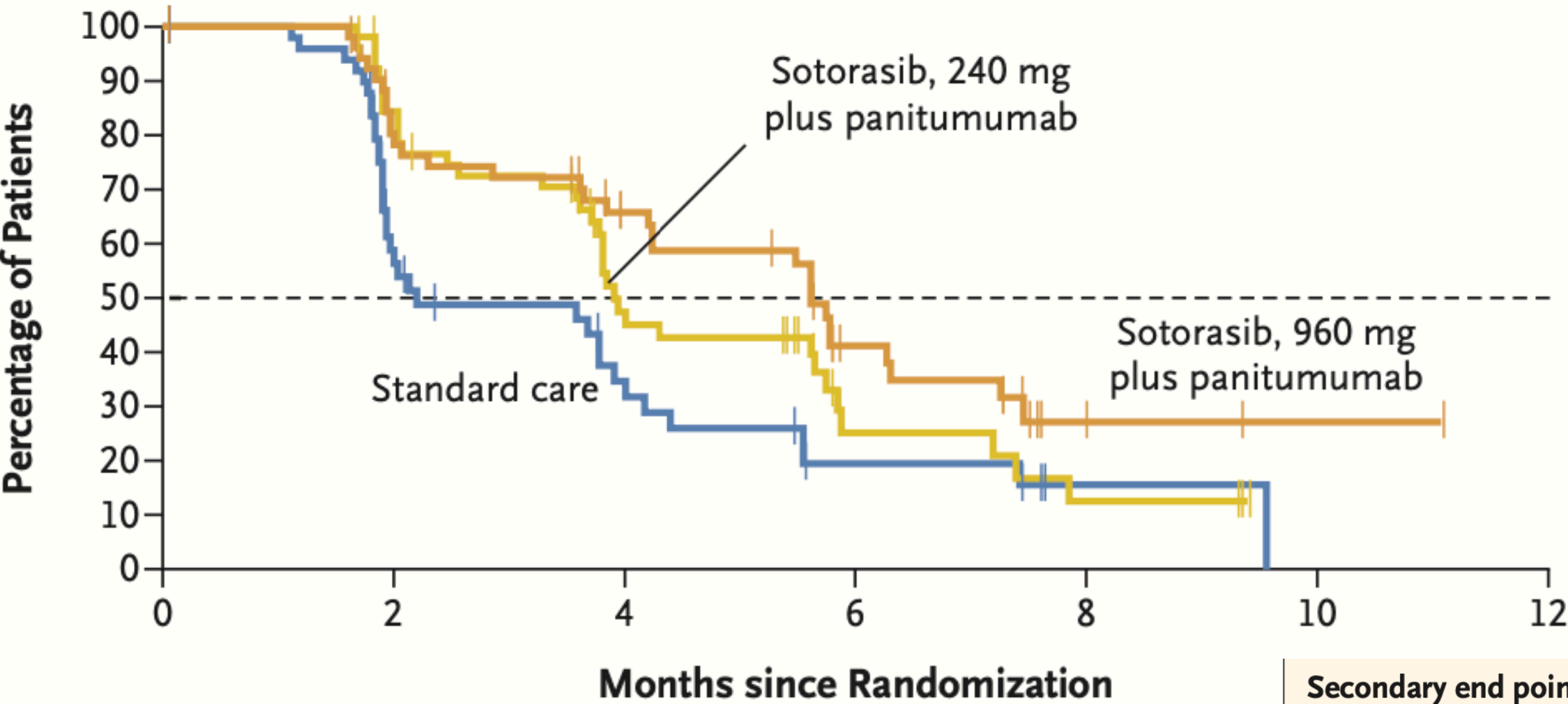
Exon 4 : K117X (K117Nc, K117Nt)

A146X (A146P, A146T, A146V)

Sotorasib plus Panitumumab in Refractory
Colorectal Cancer with Mutated KRAS G12C

M.G. Fakih, L. Salvatore, T. Esaki, D.P. Modest, D.P. Lopez-Bravo, J. Taieb, M.V. Karamouzis, E. Ruiz-Garcia, T.-W. Kim, Y. Kuboki, F. Meriggi, D. Cunningham, K.-H. Yeh, E. Chan, J. Chao, Y. Saportas, Q. Tran, C. Cremolini, and F. Pietrantonio

A Progression-free Survival (Intention-to-Treat Population)



	Median Progression-free Survival <i>mo</i>	Hazard Ratio for Disease Progression or Death (95% CI)	Two-Sided P Value
Sotorasib, 960 mg plus Panitumumab	5.62	0.49 (0.30–0.80)	0.006
Sotorasib, 240 mg plus Panitumumab	3.91	0.58 (0.36–0.93)	0.03
Standard Care	2.20		

Secondary end points			
Best overall response — no. (%)	1.9%		
Complete response	1 (1.9)	0	0
Partial response	13 (24.5)	3 (5.7)	0
Stable disease	24 (45.3)	33 (62.3)	25 (46.3)
Progressive disease	12 (22.6)	13 (24.5)	17 (31.5)
Noncomplete response or nonprogressive disease	0	2 (3.8)	1 (1.9)

Test Name	Result	Reference Range
KRAS mutation	Mutation Detected : G12X	<i>Mutation Detected: Mutation detected in specified targeted KRAS region</i> <i>No Mutation Detected: Mutation not detected in targeted KRAS region</i>

X

A

C

D

R

S

V

Method and Coverage

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The Cobas KRAS Mutation Test V.2 uses parallel specific PCR technology to detect the following 28 mutations.

Exon 2 : G12X (G12A, G12C, G12D, G12R, G12S, G12V)

G13X (G13A, G13C, G13D, G13R, G13S, G13V)

Exon 3 : A59X (A59E, A59G, A59S, A59T)

Q61X (Q61E, Q61Hc, Q61Ht, Q61K, Q61L, Q61P, Q61R)

Exon 4 : K117X (K117Nc, K117Nt)

A146X (A146P, A146T, A146V)