Queensland Molecular Tumour Board

Meeting 1

10th July 2019
Room 2004, TRI, Princess Alexandra Hospital, Woolloongabba, QLD

DR POH SEE CHOO

Medical Oncologist
Greenslopes Private Hospital
&
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Case Report

52 year old woman with metastatic breast cancer with multiple somatic gene mutations

CASE REPORT

- Initial diagnosis at age of 37
  - L breast partial mastectomy June 2004
- Histo: Multifocal grade 3 invasive ductal ca,30mm,13mm,10mm and others1-2mm.ER+ve(weak10%),PR –ve, HER 2 IHC 2+; 7/12 LN +ve
  - 6 cycles TAC followed by Tamoxifen

CASE REPORT

- Recurrence July 2009
  - Total mastectomy and axillary dissection
  - Histo: Grade 3 invasive ductal ca, 15mm and 2mm. ER+ve(strong +ve >95%),PR-ve(1%+ve), Her 2 +ve. 2LN negative
  - Staging scan- no metastatic disease
  - 6 cycles of TCH followed by Herceptin

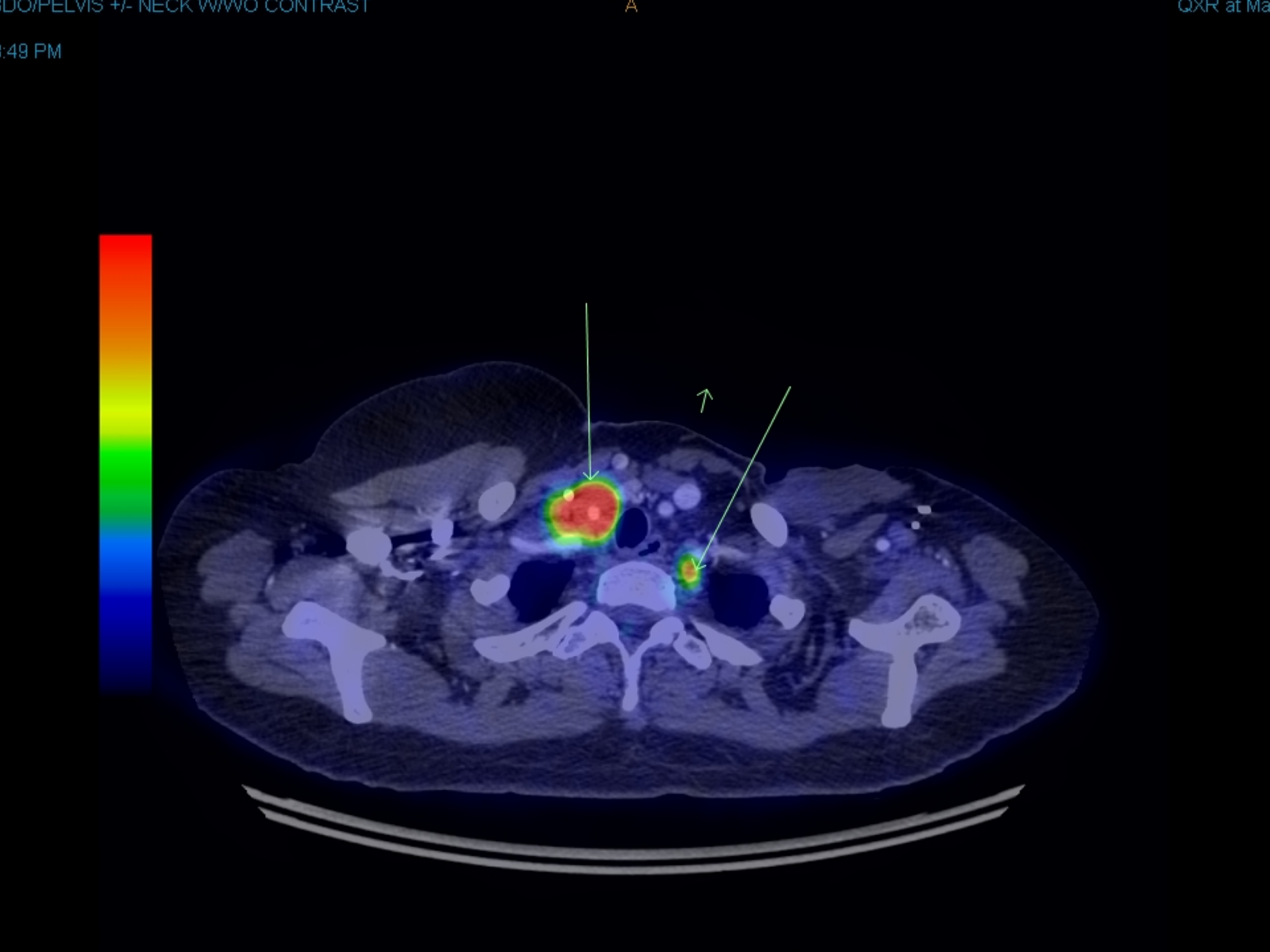
CASE REPORT

- Metastatic disease with bone mets April 2010
  - Sternal biopsy- metastatic adenocarcinoma, ER and PR negative, Her 2 +ve
  - R/V of previous scan- suggestive of bone metastasis
  - Start Zolandronic acid and continue Herceptin
  - Add Letrozole as original breast ca ER +ve
  - 2012- bilateral oophorectomy

CASE REPORT

- Progressive disease Oct 2013
  - Treatment changed to Abraxane/Herceptin
  - Completed in April 2014 and continue on Herceptin
  - Added Exemestane

- Progressive disease April 2016
  - R supraclavicular LN Bx
  - Histo: adenocarcinoma ER+ve,PR-ve HER2 +ve(SISH)
  - Scan showed extensive
  - Changed from Herceptin to Herceptin/Vinorelbine. Continue on Letrozole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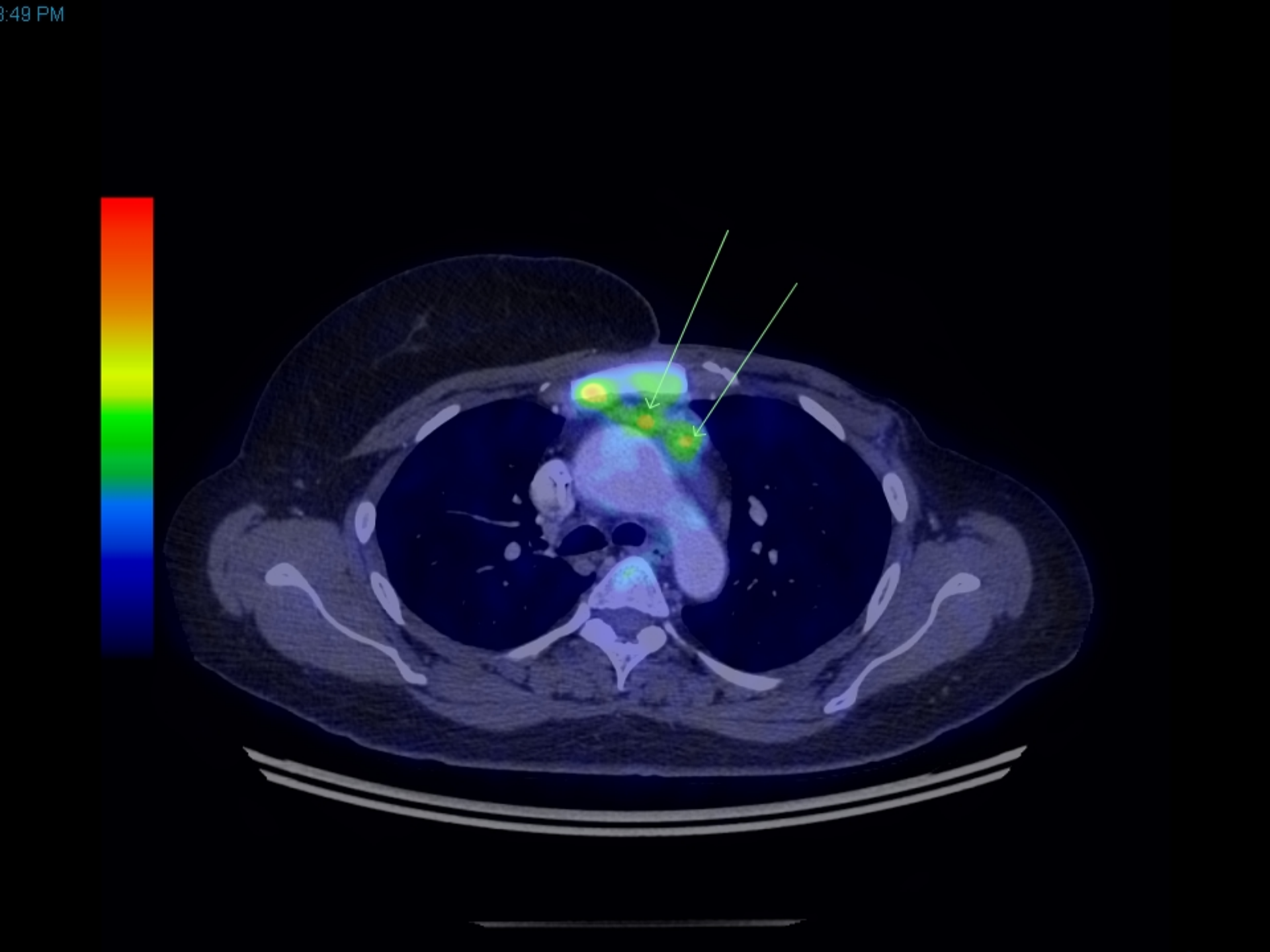
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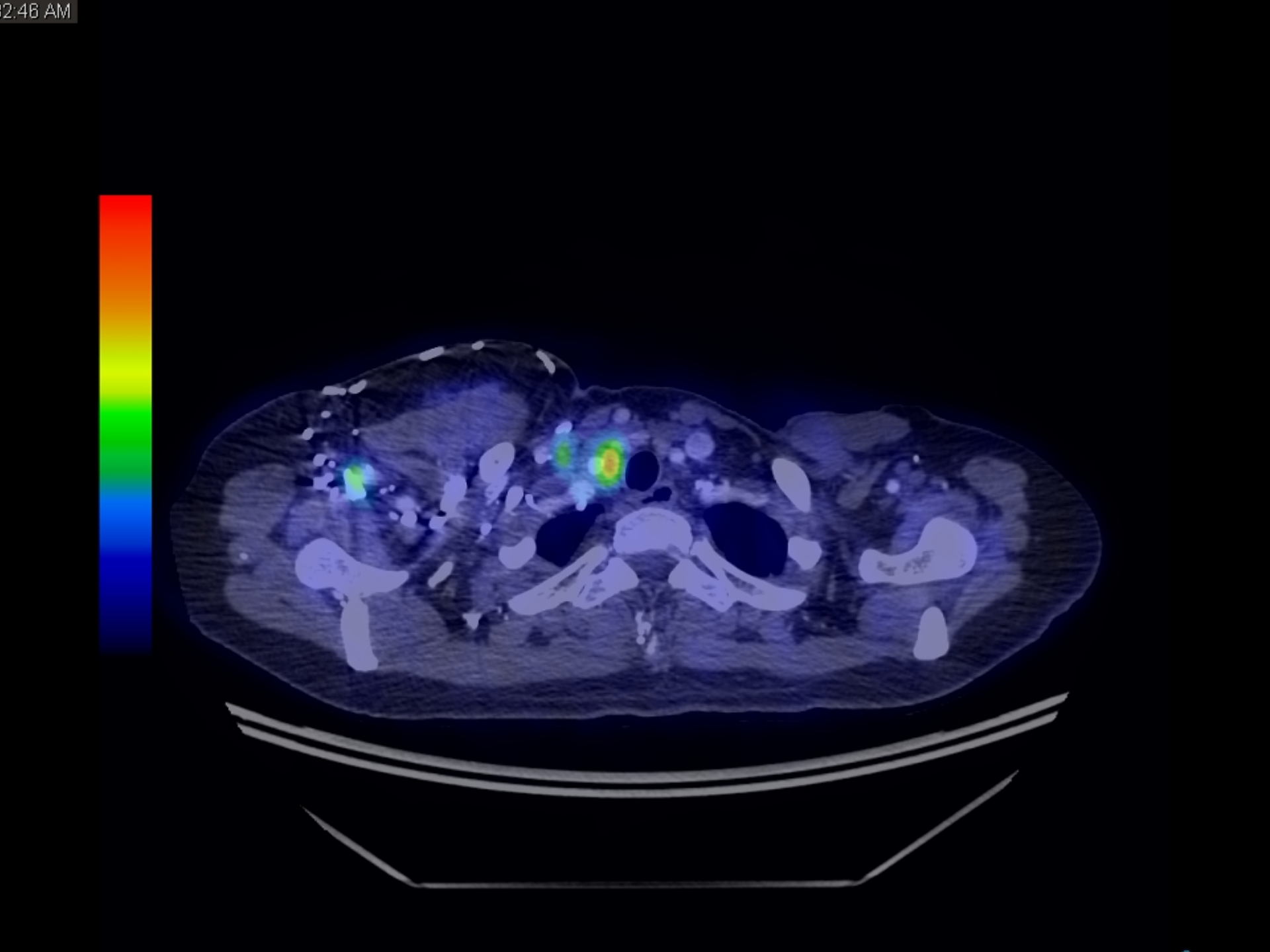
CASE REPORT

- Progression in June 2017
  - Changed to Trastuzumab emtansine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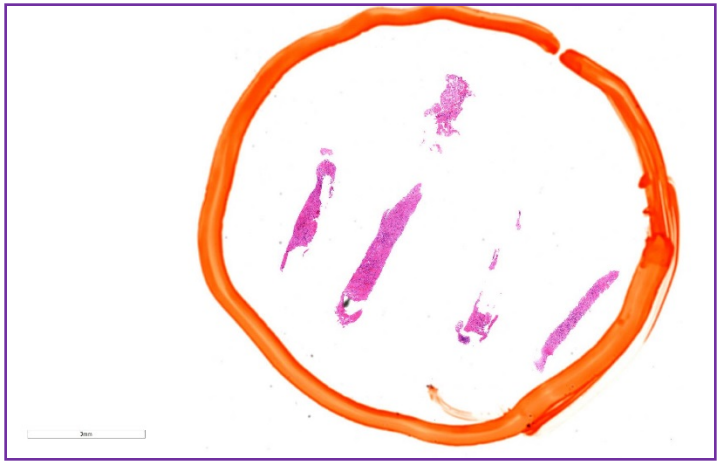
CASE REPORT

- Progression March 2018
  - Changed treatment to Gemcitabine/Herceptin
  - Genomic testing discussed

Results Summary: GFL-190100114

Percentage of Tumour: 20%
Percentage of Tumour After Enrichment: N/A



Results Summary: GFL-190100114

Somatic DNA Mutation Detected (Positive)

ERBB2 *Gene Amplification*	***CDK12*** *Gene Amplification*	***PIK3CA*** *c.3140A>G* p.H1047R	***TP53*** *c.375+1G>A* Splice Site	***SMARCA4*** *c.3108G>T* p.M1036I	**142 Genes Negative**
Oncogene Mean Coverage: 6233X Cytoband: 17q12(37868168-37882971), 14.803kb Copy Number Variation: 15.8 CNV Confidence 5%:9.63, 95%:24.12.	Oncogene Mean Coverage: 7736X Cytoband: 17q12(37618287-37687576), 69.289kb Copy Number Variation: 8.15 CNV Confidence 5%:5.8, 95%:10.9.	Oncogene Known Driver Mutation *PIK3CA* Exon 21. Mean Coverage: 6474X. Variant Allele Fraction: 26%.	Tumour Suppressor Known Driver Mutation *TP53* Intron 4. Mean Coverage: 5101X. Variant Allele Fraction: 34%.	Chromatin Remodelling Predicted Driver Mutation *SMARCA4* Exon 22. Mean Coverage: 294X. Variant Allele Fraction: 16%.	Mean Coverage: 727X.

Tumour Mutational Load:

TML Low

Mutation Load per MB: 4.03.

The Possible Response Rate to single agent Immune Checkpoint Inhibitors is based on published data using TML analysis, *in vivo* mouse models and clinical trial data (Antonia, Goldberg et al. 2016, Tamkus and Joginpally 2016, Birendra, Hwang et al. 2017, Carbone, Reck et al. 2017, Crosby, Wei et al. 2017, Dua and Tan 2017, Heong, Ngoi et al. 2017, Skoulidis, Hellmann et al. 2017, Somasundaram and Burns 2017, Yarchoan, Hopkins et al. 2017, Overman, Lonardi et al. 2018, Rizvi, Sanchez-Vega et al. 2018).

Results Summary: GFL-190100114

Probable Germline DNA Mutation (Positive)

CDK12
c.3734C>T
p.Pro1245Leu

Genomic Stability
CDK12 Exon 13.
Mean Coverage: 722X.
Variant Allele Fraction: 69%.

PTCH1
c.1994G>A
p.Arg665His

Tumour Suppressor
PTCH1 Exon 14.
Mean Coverage: 580X.
Variant Allele Fraction: 71%.

Somatic RNA Fusion – NOT Detected (Negative)

51 Genes Negative

Total Reads: 2864368X

Results Summary: GFL-190100113

The *PIK3CA c.3140A>G;* p.H1047R mutation identified in the tumour sample was identified in the cfTNA sample. *ERBB2* (*HER2*) gene amplification was not identified in the cfTNA and this may be related to therapy changes, tumour heterogeneity or clonal evolution. Clinicopathological correlation is required.

PIK3CA
c.3140A>G
p.H1047R

Oncogene
Known Driver Mutation
PIK3CA Exon 21.
Molecular Depth: 1444X.
Mean Depth: 57289X.
Variant Allele Fraction: 0.554%.
Limit of Detection: 0.15%

ERBB2
Amplification Not Detected

Oncogene
Cytoband: 17q12(37863180-37882971), 19.791kb
Copy Number Variation: 2.02
Mean Depth: 70255X.

50 Genes Negative

Mean Coverage: 57499X.

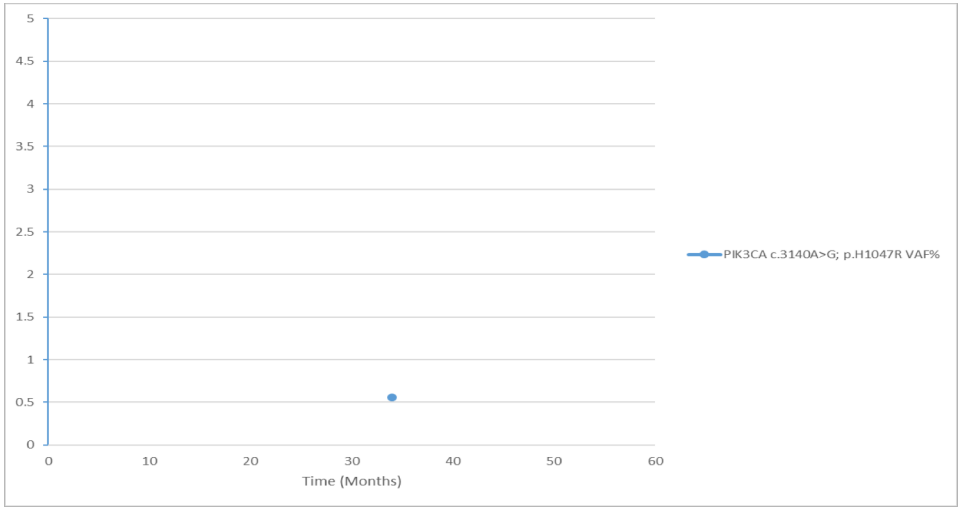


Figure 1: Graph of results for cfDNA showing cell-free tumour variant allele fraction (VAF).