

# Approach to Salivary Gland tumors- Role of anti-Her2 therapy

Dr Bharat Bhosale

Department of Medical Oncology

Bombay Hospital Mumbai

# Case capsule

- 62/M
- HTN/IHD
- Presented with rt. Sided neck swelling
- FNAC: adenocarcinoma
- Came for second opinion
- Clinical evaluation revealed Rt SCLN and cutaneous induration over Sternal area
- Joint MDT( Jaslok)
- Biopsy by advised by MDT discussion Dr Rakesh /Dr Bharat/Dr Nikhil
- Ref to Med Onco

# Biopsy-→ IHC

## **CLINICAL DATA**

Right parotid mass with soft tissue extension, supraclavicular lymphadenopathy, liver & osseous lesions.

## **GROSS APPEARANCE**

Number of containers received : 1.

Biopsy in formalin : Yes.

Received multiple linear cores of tissue measuring approximately 0.1 to 0.5 cm. Submitted entirely in 3 paraffin blocks labelled as 1 to 3.

## **MICROSCOPIC APPEARANCE**

The core biopsy reveals a high grade ductal adenocarcinoma. Foci of necrosis & squamous differentiation are noted.

The tumor cells express cytokeratin, p63 (focal) & androgen receptor.

**Age** : 62 years      **Gender** : Male

**Referred by** : Dr. Bharat Bhosale

**Accessioned on** : 19 Apr 2021 03:56 PM

**Reported on** : 20 Apr 2021 03:23 PM

**Nature of material** : 1 paraffin block (21W-3939- 1) of parotid tumor for hormone receptor studies (ER/PR/Her2neu)

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## **IMPRESSION**

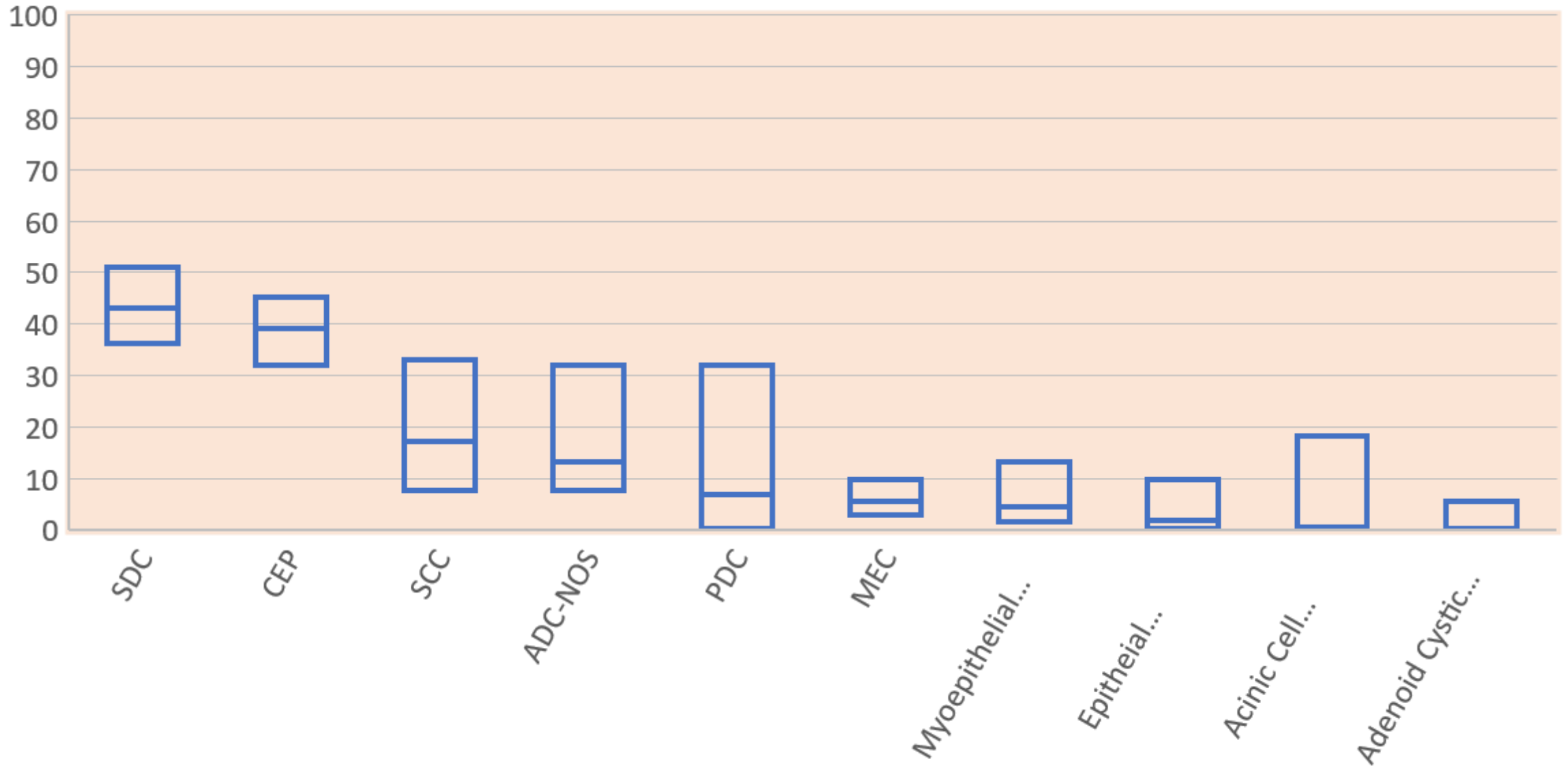
**Hormone receptor studies on parotid tumor on block no. 21W-3939-1 : -**

**ER : Negative.**

**PR : Negative.**

**Her2neu : Positive, score 3 (strong, more than 90% of tumor cells).**

## HER-2 NEU POSITIVITY VERSUS HISTOLOGY



UIDPET464421  
\*4/12/1959, M, 62Y

STUDY 4/12/2021  
7 IMA n.a.

INFINITY MEDICAL CENTRE SE

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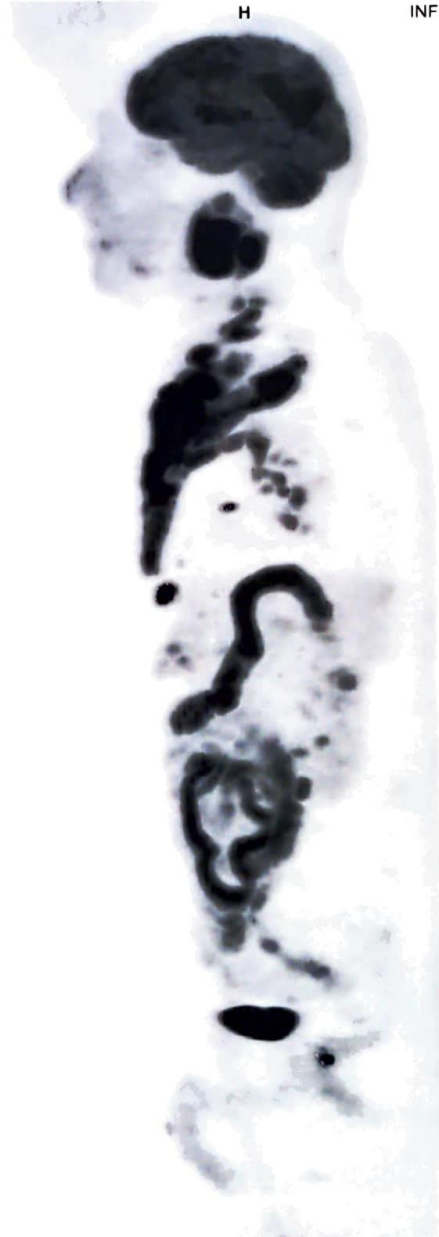
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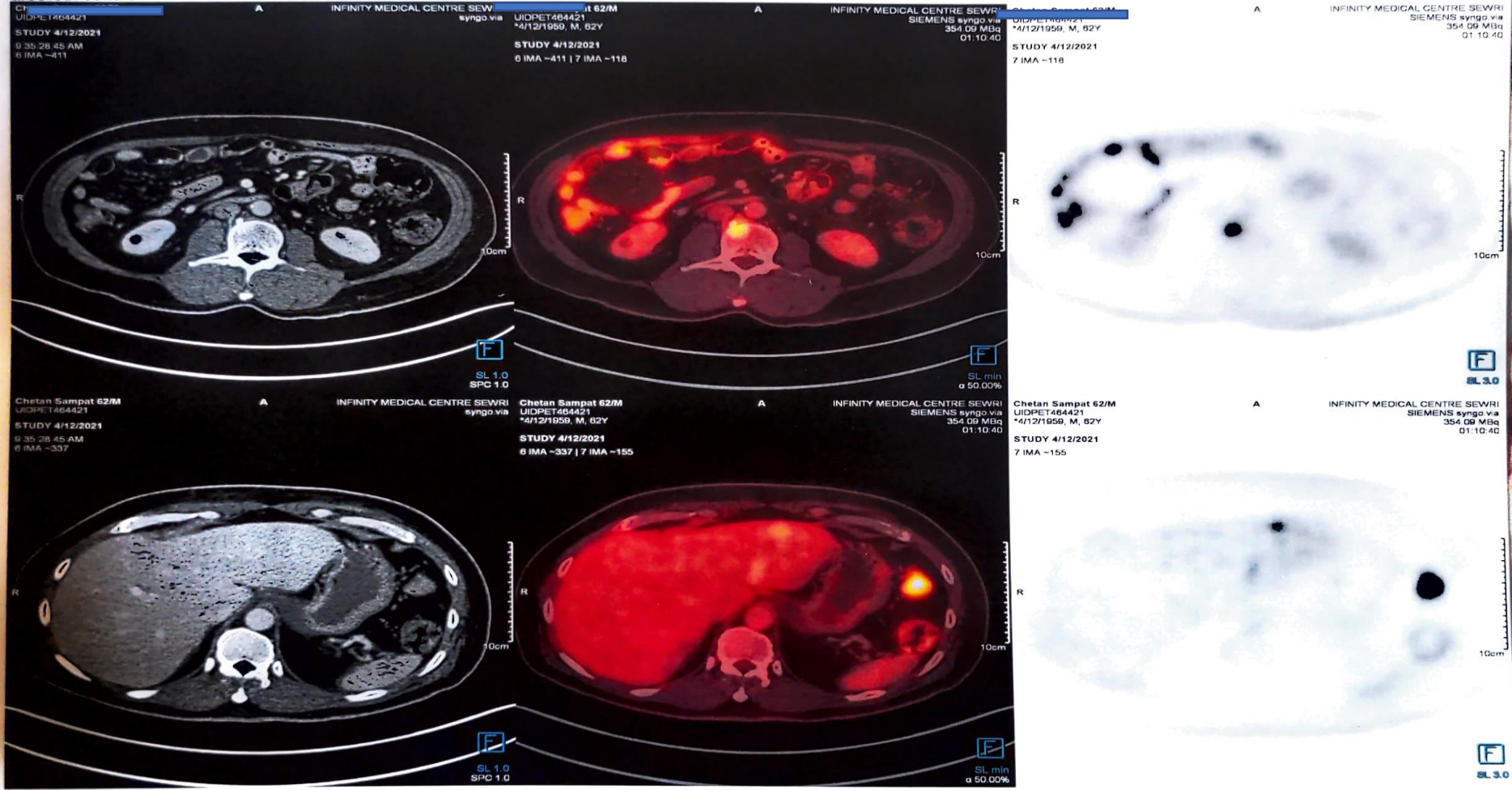
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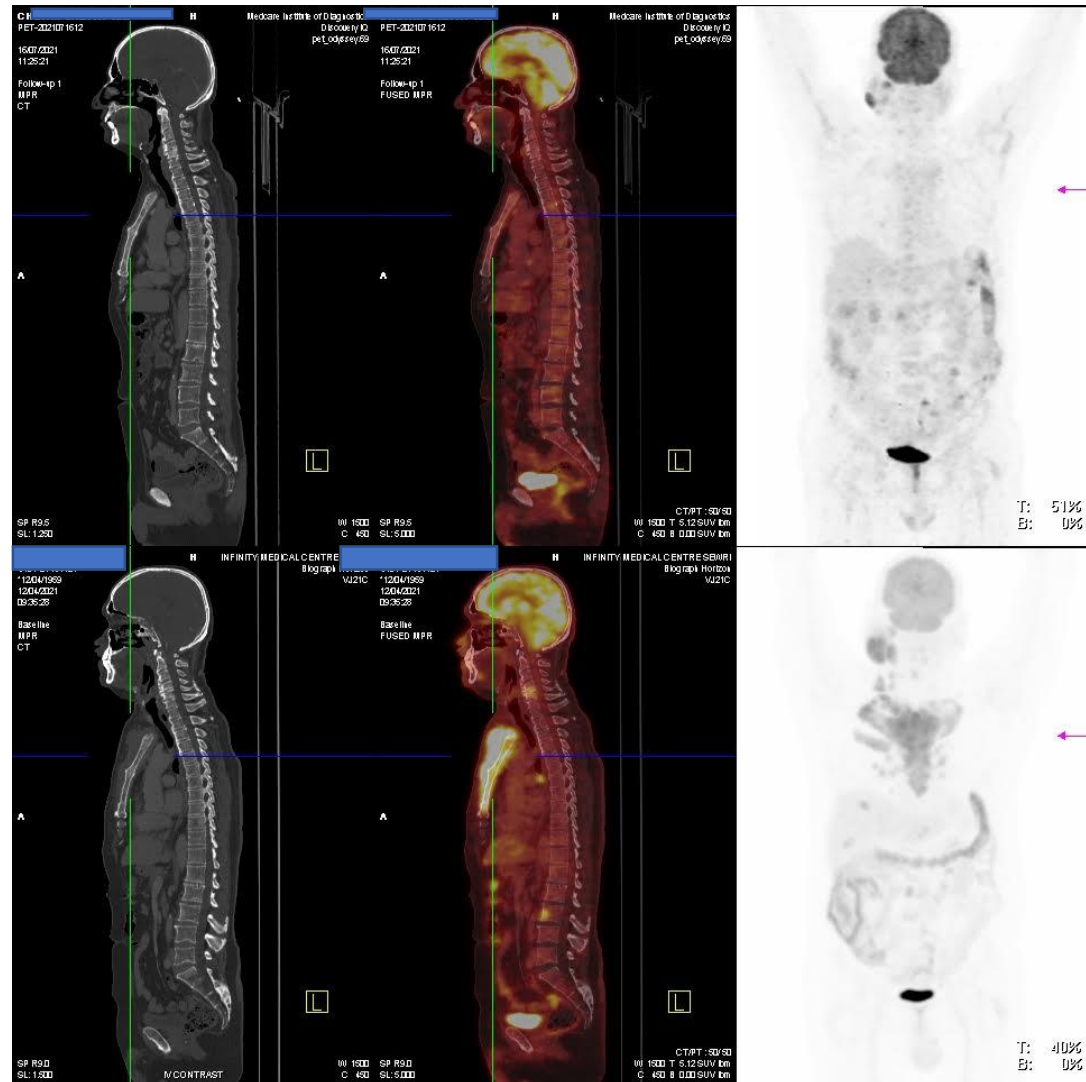
L



# Post 3 cycles Pall chemo + Her 2 targeted therapy

1. Post 6 cycles TPH-  
→ CR

2. Maintenance PH till  
OCT 2022 CR  
maintained




[Journal of Clinical Oncology](#) > [List of Issues](#) > [Volume 37, Issue 2](#) >

ORIGINAL REPORTS | [Head and Neck Cancer](#)

# Phase II Trial of Trastuzumab and Docetaxel in Patients With Human Epidermal Growth Factor Receptor 2–Positive Salivary Duct Carcinoma



Check for updates

[Hideaki Takahashi](#), MD, PhD<sup>1</sup>; [Yuichiro Tada](#), MD<sup>1</sup> ; [Takashi Saotome](#), MD<sup>2</sup>; [Kohei Akazawa](#), PhD<sup>3</sup>; [Hiroya Ojiri](#), MD, PhD<sup>4</sup>; [Chihiro Fushimi](#), DDS, PhD<sup>1</sup>; ...

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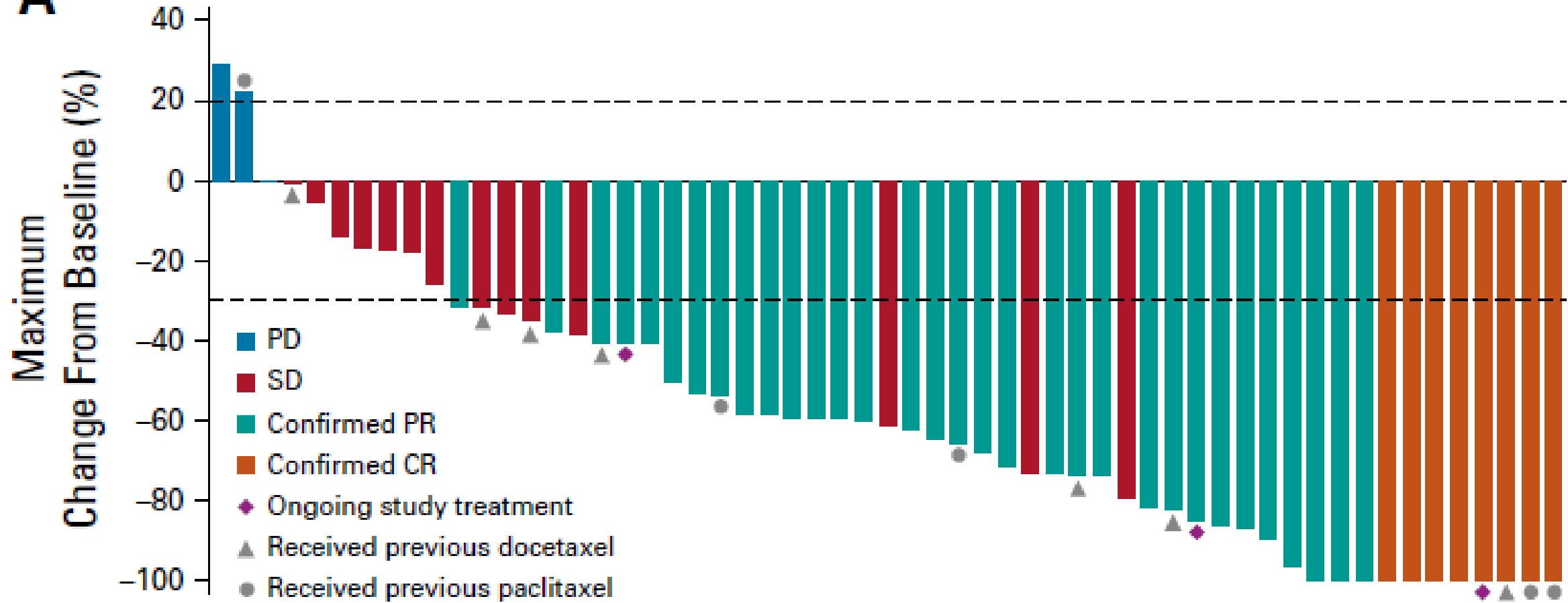
H.T. and Y.T. contributed equally to this study.



Unknown	16 (28)
Sample used for HER2 analysis	
Primary tumor	50 (88)
Cervical lymph node	4 (7)
Metastatic lesion	3 (5)
HER2 status	
Positive*	57 (100)
Immunohistochemistry score	
3+	52 (91)
2+	5 (9)
FISH HER2/CEP17 ratio	
≥ 2.0	51 (89)
< 2.0	5 (9)
Not available	1 (2)
<i>HER2</i> gene copy number	
< 4.0	4 (7)
≥ 4.0, < 6.0	7 (12)
≥ 6.0, < 12.0	27 (47)
≥ 12.0	18 (32)
Not available	1 (2)

FISH status

Previous agents	
Platinum	16 (28)
Docetaxel	7 (12)
Paclitaxel	5 (9)
S1	4 (7)
ADT	3 (5)
Other agents	11 (19)
No. of previous lines of systemic therapy for metastatic disease	
1	9 (16)
2	2 (4)
3	3 (5)
4	1 (2)
Previous chemotherapy regimen received for metastatic disease	
Paclitaxel + carboplatin	5 (9)
S1 monotherapy	4 (7)
Docetaxel + carboplatin	2 (4)
Bicalutamide + leuprorelin	2 (4)
Other regimens	12 (21)
Median interval from previous systemic therapy, weeks (range)	18 (2-69)

**A**

**TABLE 2.** Treatment Efficacy

<b>Outcome</b>	<b>All patients (N = 57)</b>
Complete response	8 (14.0)
Partial response	32 (56.1)
Stable disease	14 (24.6)
Progressive disease	3 (5.3)
Objective response*	40 (70.2)
95% CI, %	56.6 to 81.6
Stable disease $\geq$ 24 weeks	8 (14.0)
Clinical benefit†	48 (84.2)
95% CI, %	72.1 to 92.5
Median progression-free survival, months	8.9
95% CI, months	7.8 to 9.9
Median overall survival, months	39.7
95% CI, months	(NR)

## ORIGINAL ARTICLE

# Targeted therapy for advanced salivary gland carcinoma based on molecular profiling: results from MyPathway, a phase IIa multiple basket study

R. Kurzrock<sup>1\*</sup>, D. W. Bowles<sup>2</sup>, H. Kang<sup>3†</sup>, F. Meric-Bernstam<sup>4</sup>, J. Hainsworth<sup>5,6</sup>, D. R. Spiegel<sup>5,6</sup>, R. Bose<sup>7</sup>, H. Burris<sup>5,6</sup>, C. J. Sweeney<sup>8</sup>, M. S. Beattie<sup>9</sup>, S. Blotner<sup>10</sup>, K. Schulze<sup>11</sup>, V. Cuchelkar<sup>12</sup> & C. Swanton<sup>13</sup>

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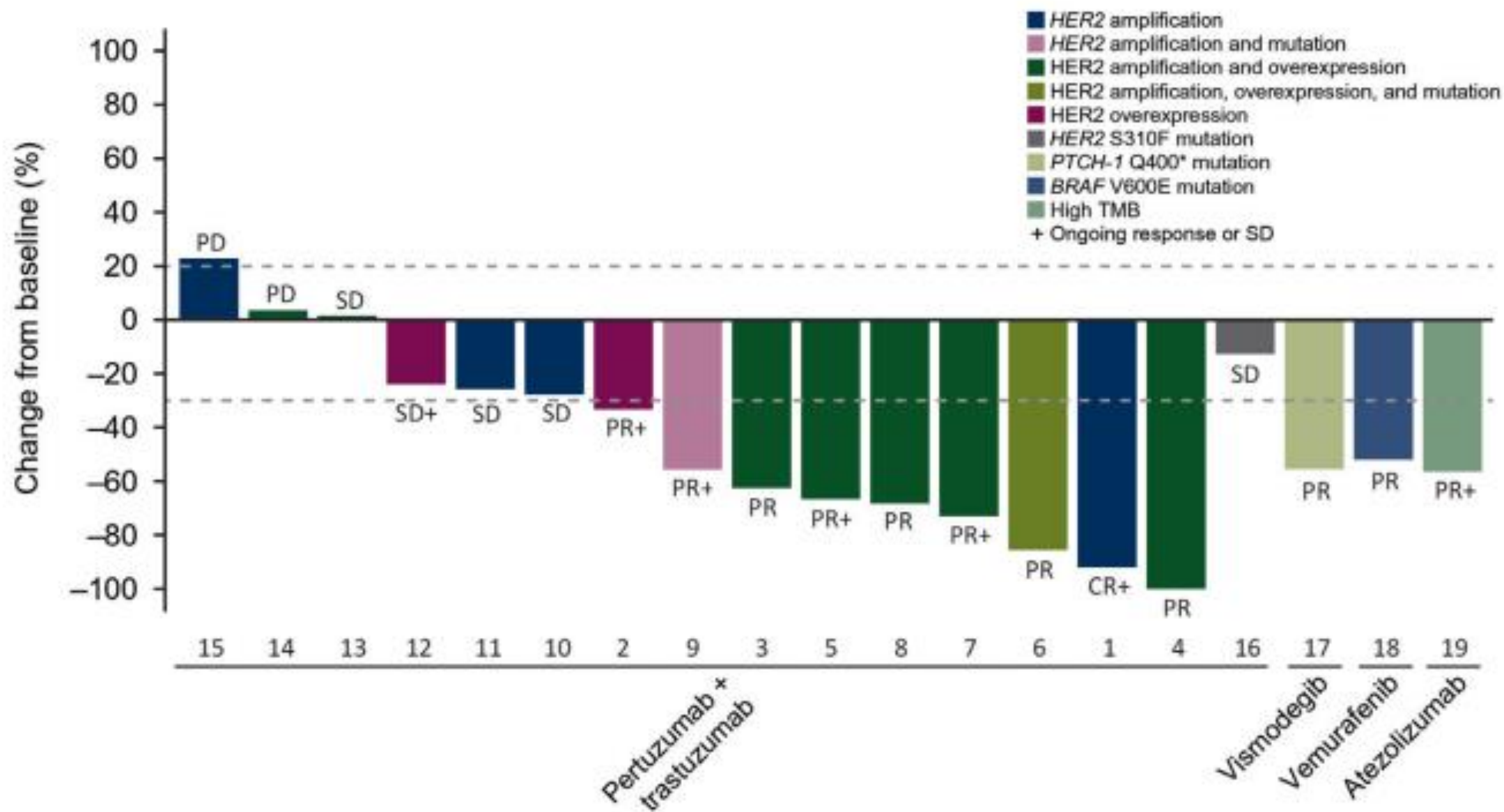
Available online 24 January 2020

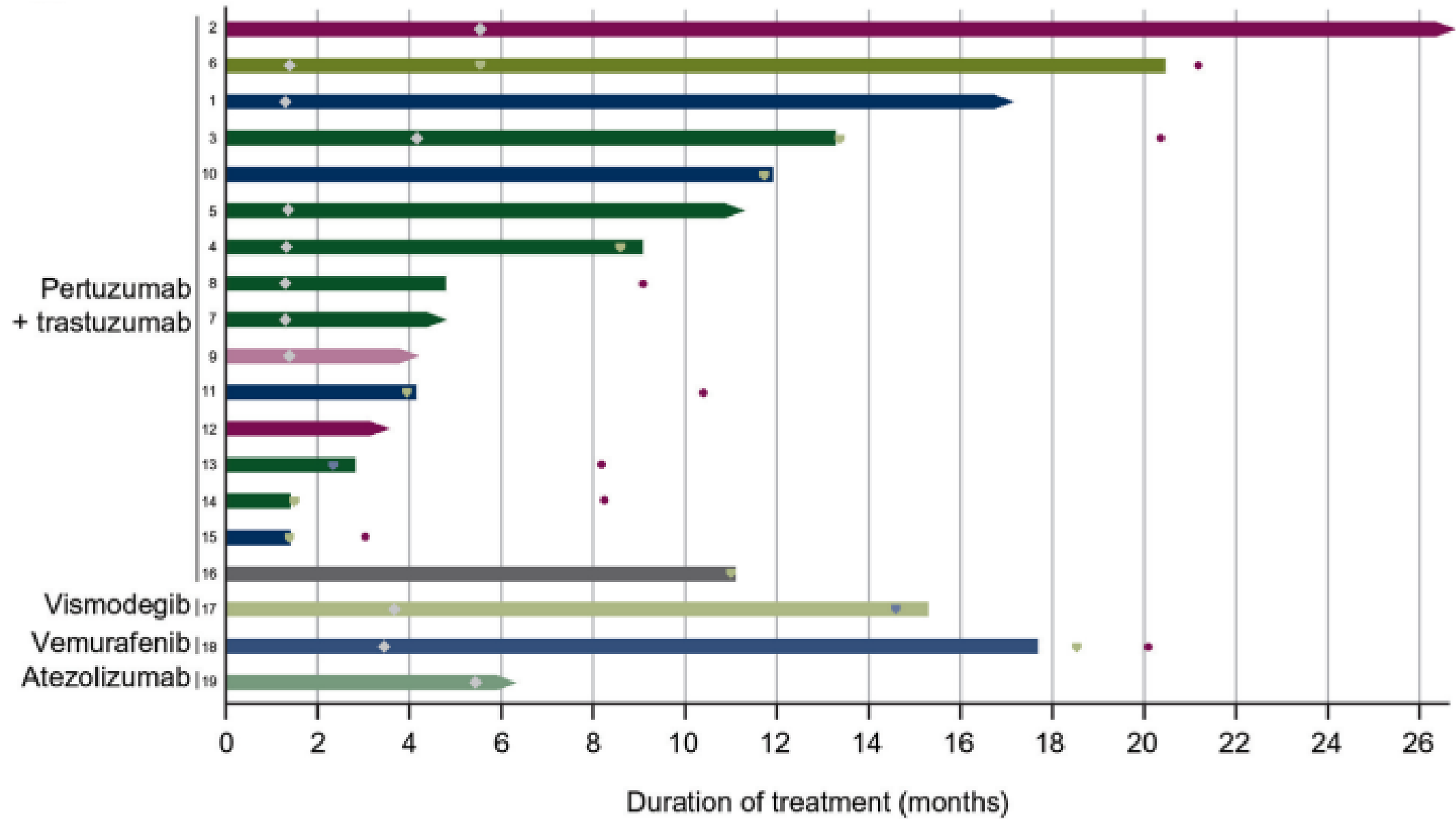
**Table 1. Baseline demographics and clinical characteristics by patient**

Pt	Sex	Age, years	Race	ECOG PS	Histology	Grade	Stage	Alteration	Testing platform <sup>a</sup>	Previous lines of therapy <sup>b</sup>	Sites of metastasis
<b>HER2 amplification and/or overexpression: treated with pertuzumab + trastuzumab</b>											
1	M	59	White	0	Salivary duct adenocarcinoma	G3	IV	HER2 amplification	NGS (copy number = 15)	1	Brain, lung, LN
2	M	80	White	1	Adenocarcinoma	G2	IVA	HER2 overexpression	IHC (3+)	1	Bone, LN
3	M	55	Black/African American	2	Unspecified carcinoma	G3	IVA	HER2 amplification + overexpression	FISH/CISH (ratio = 7.3), IHC (3+)	2	Bone, lung, LN
4	M	70	White	1	Invasive ductal carcinoma	G4	IV	HER2 amplification + overexpression	FISH/CISH (ratio = 2.4), IHC (3+)	1	Bone, liver, LN
5	M	73	White	1	Adenocarcinoma	G3	IV	HER2 amplification + overexpression	FISH/CISH (ratio = 9.9), IHC (3+)	1	Bone, LN, spleen
6	M	47	White	1	Adenocarcinoma	G3	IVC	HER2 amplification, overexpression + mutation	NGS (copy number gain; L755F and D769H mutations), IHC (3+)	0	Bone, LN
7	M	61	White	1	Unspecified carcinoma	G3	III	HER2 amplification + overexpression	NGS (copy number = 94); IHC (3+)	0	Liver, lung
8	F	54	White	0	Adenocarcinoma	G3	IV	HER2 amplification + overexpression	NGS (copy number = 104), IHC (3+)	0	Liver, LN
9	M	54	Other	1	Unspecified carcinoma	G3	III	HER2 amplification + mutation	FISH/CISH (ratio = 5.5), NGS (G776V mutation)	0	Bone, lung, LN
10	F	75	Asian	0	Adenocarcinoma	G3	IVA	HER2 amplification	NGS (copy number gain)	0	Lung
11	M	70	White	1	Unspecified carcinoma	G1	IVC	HER2 amplification	NGS (copy number = 60)	2	Bone, liver, lung, LN, intraorbital
12	M	37	White	1	Adenocarcinoma	GX	IV	HER2 overexpression	IHC (3+)	1	Bone, liver
13	M	62	American Indian or Alaska native	1	Mucoepidermoid carcinoma	G3	III	HER2 amplification + overexpression	FISH/CISH (ratio = 7.8), NGS (copy number = 20), IHC (3+)	3	Adrenal gland, liver, lung, LN
14	M	48	Asian	1	Invasive ductal carcinoma	G4	IVA	HER2 amplification + overexpression	FISH/CISH (ratio = 7.2), IHC (3+)	1	Brain, lung, LN
15	F	44	White	2	Adenocarcinoma	G3	IV	HER2 amplification	NGS (copy number = 15)	2	Brain, chest wall, left eye, liver, LN, neck (subcutaneous tissue), parapharyngeal mucosa
<b>HER2 mutation: treated with pertuzumab + trastuzumab</b>											
16	M	68	White	0	Adenocarcinoma	G3	III	HER2 mutation	NGS (S310F mutation)	0	Lung, LN, mediastinum

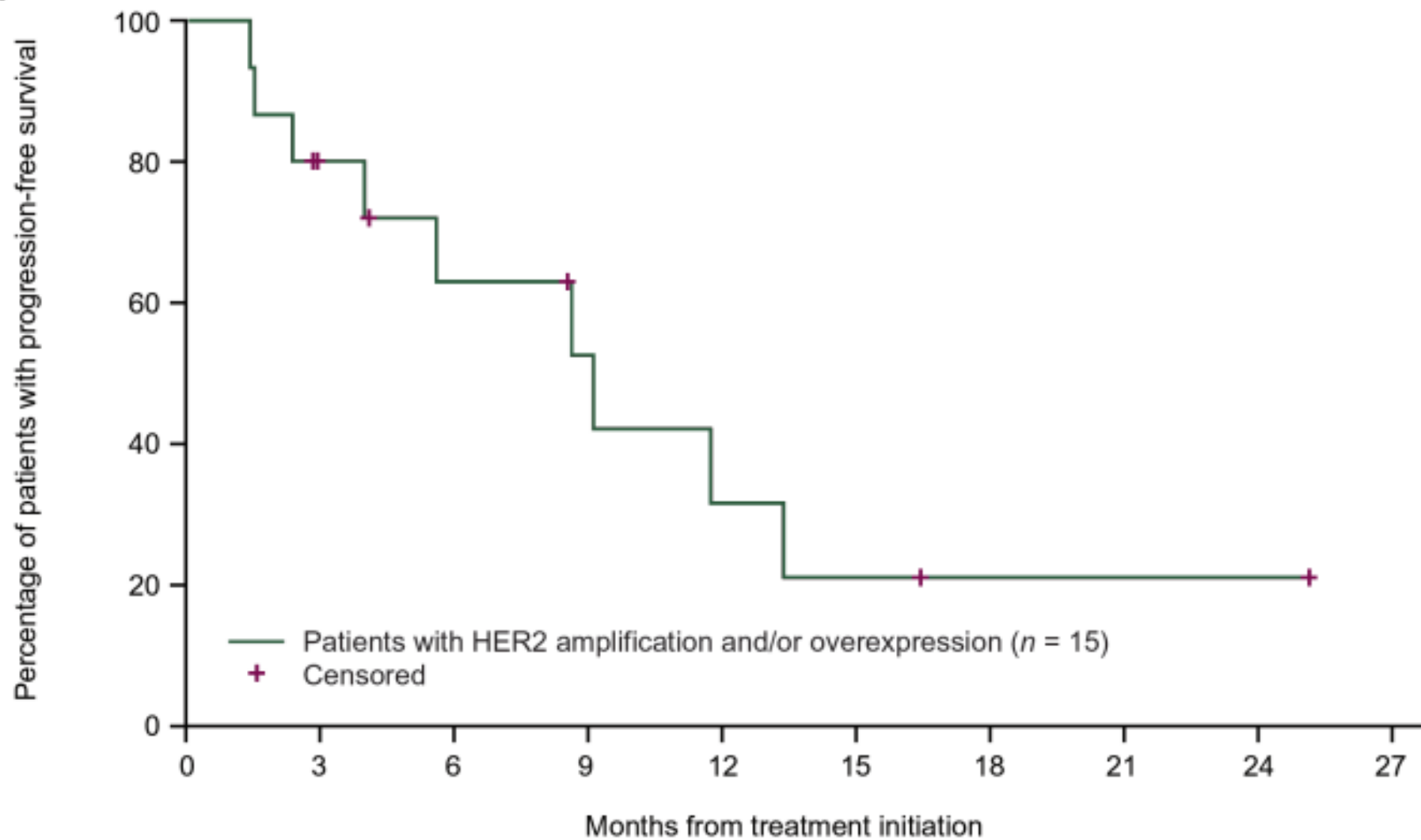
**Table 2. Clinical outcomes by patient**

Pt	Alteration	Time on treatment, months	Best response	Duration of response, months	Duration of SD, months	Best change in target lesion size from baseline, %	PFS, months	OS, months
<b>HER2 amplification and/or overexpression: treated with pertuzumab + trastuzumab</b>								
1	HER2 amplification	16.5+	CR	15.2+	—	−91.7 <sup>a</sup>	16.5+	16.5+
2	HER2 overexpression	26.1+	PR	19.7+	—	−33.3	25.2+	26.1+
3	HER2 amplification and overexpression	12.6	PR	9.2	—	−62.5	13.4	20.4
4	HER2 amplification and overexpression	8.3	PR	7.3	—	−100.0 <sup>b</sup>	8.6	14.9+
5	HER2 amplification and overexpression	10.6+	PR	7.2+	—	−66.7	8.5+	10.6+
6	HER2 amplification, overexpression, and mutation (L755F and D769H)	19.8	PR	4.2	—	−85.7	5.6	21.2
7	HER2 amplification and overexpression	4.1+	PR	2.8+	—	−73.0	4.0+	4.1+
8	HER2 amplification and overexpression	4.1 <sup>c</sup>	PR	2.7	—	−68.2	9.1	9.1
9	HER2 amplification and mutation (G776V)	3.5+	PR	1.4+	—	−55.7	2.8+	3.5+
10	HER2 amplification	11.2	SD	—	11.7	−27.9	11.7	14.0+
11	HER2 amplification	3.5	SD	—	3.9	−25.6	3.9	10.4
12	HER2 overexpression	2.9+	SD	—	2.9+	−24.3	2.9+	2.9+
13	HER2 amplification and overexpression	2.1	SD	—	2.3	1.4	2.3	8.2
14	HER2 amplification and overexpression	0.7	PD	—	—	3.6	1.5	8.3
15	HER2 amplification	0.7	PD	—	—	22.5	1.4	3.1
<b>HER2 mutation: treated with pertuzumab + trastuzumab</b>								
16	HER2 mutation (S310F)	10.4	SD	—	11.0	−12.8	11.0	13.7+







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Patients at risk

15

10

7

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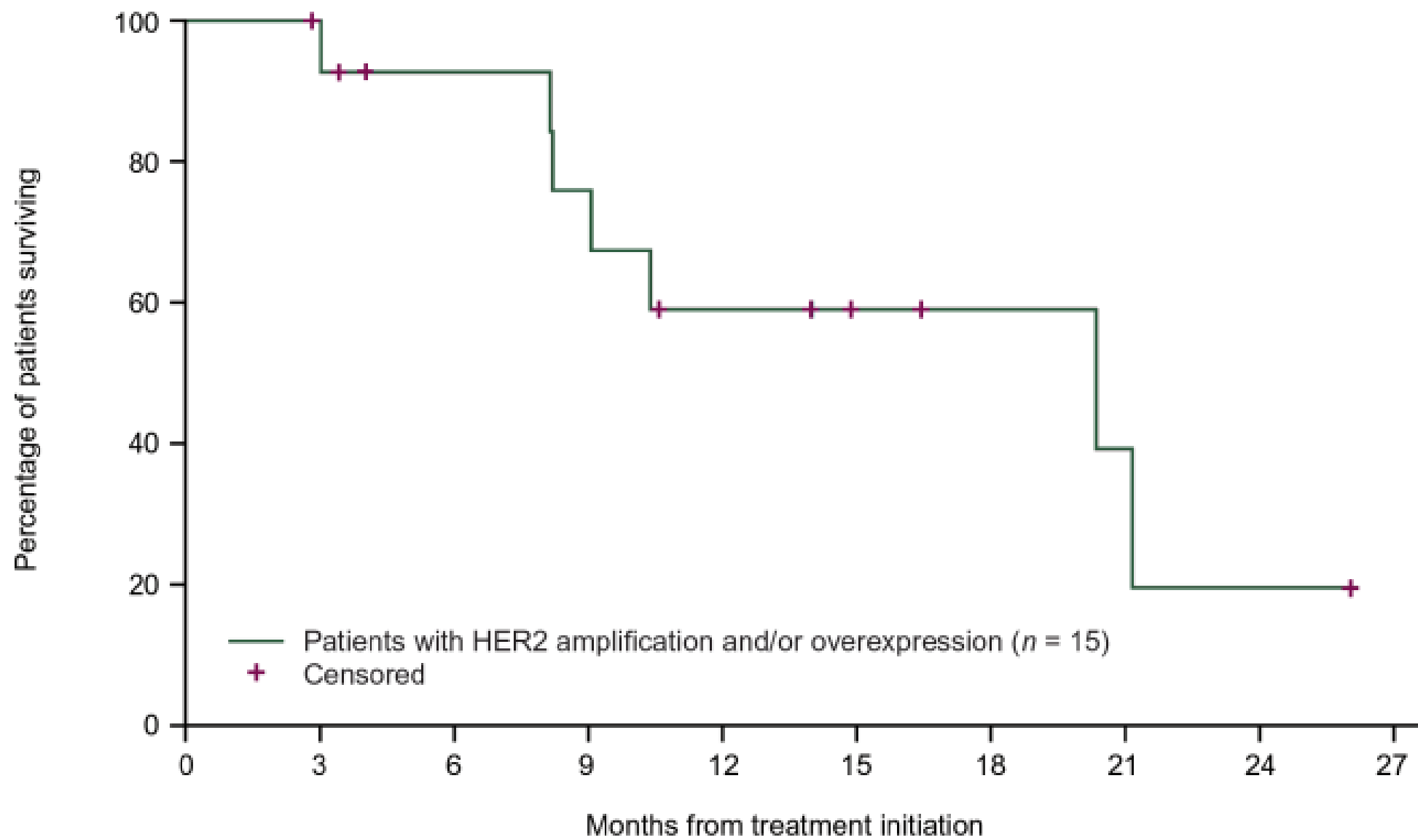
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Patients at risk 15 14 11 9 6 4 3 2 1

HEAD AND NECK CANCER

# Ado-trastuzumab emtansine in patients with *HER2* amplified salivary gland cancers (SGCs): Results from a phase II basket trial.



Check for updates

[Bob T. Li](#), [Ronglai Shen](#), [Michael Offin](#), [Darren J. Buonocore](#), [Mackenzie L. Myers](#), [Aishwarya Venkatesh](#), ...

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# Baseline & Response

- 10 patients with *HER2* amplified SGCs were treated.
- The median age was 65 (range 36-90 years), 90% were male.
- The median lines of prior systemic therapy was 2 (range 0-3).
- ORR was 90% (9/10, 95% CI 56-100%) including 5 complete responses after prior trastuzumab, pertuzumab and anti-androgen therapy

# Efficacy & Adverse events

- After a median follow up period of 12 months (range 4-20 months), median DOR (range 2-19+) and median PFS (95% CI 4–22+ months) were not reached.
- Toxicities included grade 1 or 2 infusion reaction, thrombocytopenia and transaminitis; there were no treatment related deaths.



## Oral Oncology

Volume 125, February 2022, 105703



Case series of docetaxel, trastuzumab, and pertuzumab (DTP) as first line anti-HER2 therapy and ado-trastuzumab emtansine (T-DM1) as second line for recurrent or metastatic HER2-positive salivary duct carcinoma

M.J.M. Uijen <sup>a, 1</sup>, G. Lassche <sup>a, 1</sup>, A.C.H. van Engen-van Grunsven <sup>b</sup>, C.M.L. Driessen <sup>a</sup>, C.M.L. van Herpen <sup>a</sup>



PatientNo.	Age	Gender	Primary tumor	Prior treatments	Disease distribution	Sites of DM	HER2 status assessed on	HER IHC	HER FISH	AR IHC †
1	48	F	Parotid gland	Surgery + PORT	DM	Lung	Primary tumor	3+	amplified	positive
2	64	M	Parotid gland	Surgery + PORT Palliative ADT	DM	Lung, liver, lymph node	Primary tumor	3+	amplified	positive
3	54	M	Parotid gland	Surgery + PORT Palliative ADT	DM	Lung, liver, bone	Bone metastasis	3+	amplified	positive
4	59	M	Parotid gland	Surgery Palliative ADT	DM	Brain, bone, lymph node	Primary tumor	2-3+	amplified	positive
5	54	F	Parotid gland	Palliative ADT	LR + DM	Lung, liver, lymph node	Liver metastasis	2-3+	amplified	positive
6	51	M	Parotid gland	-	LR	-	Primary tumor	2-3+	amplified	positive
7	55	M	Parotid gland	Surgery	DM	Brain, lung, lymph node	Lung metastasis	3+	amplified	positive
8	66	F	Parotid gland	Surgery + PORT Adjuvant ADT	DM	Lung	Primary tumor	3+	amplified	positive
9	75	M	Submandibular gland	Surgery + PORT Adjuvant ADT	DM	Lung, lymph node	Primary tumor	3+	amplified	positive
10	64	M	Parotid gland	Palliative chemo† Palliative ADT	LR + DM	Lymph node	Lymph node metastasis	3+	amplified	positive
11	61	M	Parotid gland	Surgery + PORT Adjuvant ADT	DM	Liver	Liver metastasis	2-3+	amplified	positive
12	62	M	Parotid gland	Surgery + PORT Palliative Rx	LR + DM	Lymph node, brain	Primary tumor	3+	amplified	positive
13	67	M	Parotid gland	Surgery + PORT Palliative ADT	LR + DM	Lung, pancreas	Primary tumor	3+	amplified	positive

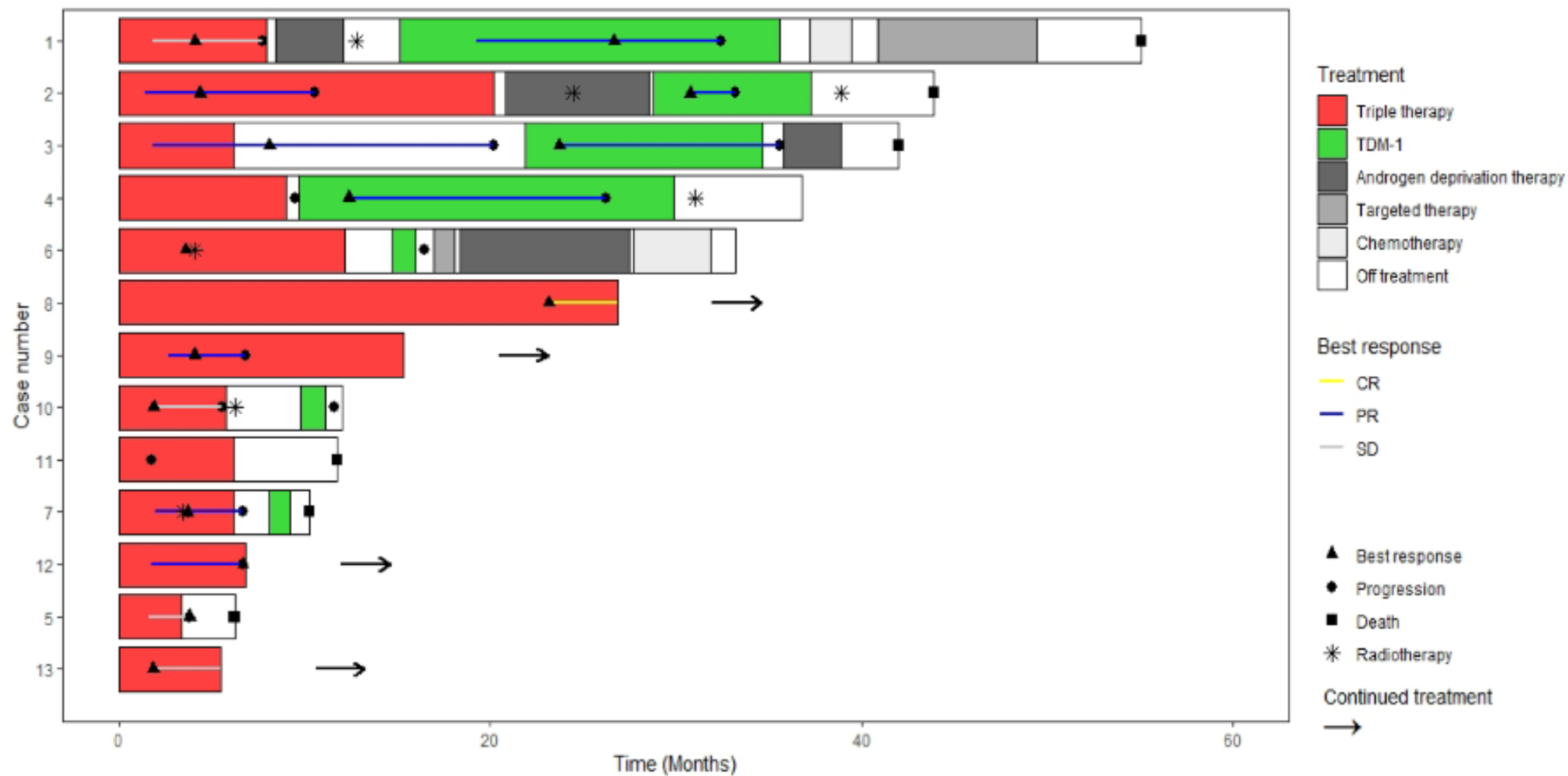



Figure 1. Swimmers plot, graphically summarizing treatment and response information per individual case.



## Response to HER2 targeted therapy.

Patient No.	First-line HER2 targeted treatment (DTP therapy)	Best response	Best percentage change in target lesions	Duration of response	Second-line HER2 targeted treatment (T-DM1)	Best response	Best percentage change in target lesions	Duration of response
1	Docetaxel + trastuzumab + pertuzumab	SD	-17%	7.7 mo	T-DM1	PR	-78%	17.3 mo
2	Docetaxel + trastuzumab + pertuzumab	PR	-62%	10.6 mo	T-DM1	PR	-32%	4.4 mo
3	Docetaxel + trastuzumab + pertuzumab	PR	-100%	20.2 mo	T-DM1	PR	-42%	13.7 mo
4	Docetaxel + trastuzumab + pertuzumab	IR/SD*	N.A.	9.5 mo	T-DM1	PR	-40%	16.6 mo
5	Docetaxel + trastuzumab + pertuzumab	SD	-27%	3.8 mo	-	-	-	-
6	Docetaxel + trastuzumab + pertuzumab	PR	-33%	Unclear <sup>†</sup>	T-DM1	PD	+22%	1.8 mo
7	Docetaxel + trastuzumab + pertuzumab	PR	-45%	6.7 mo	T-DM1	PD	Unclear <sup>†</sup>	Unclear <sup>†</sup>
8	Docetaxel + trastuzumab + pertuzumab	CR	-100%	Ongoing at 26.8 mo	-	-	-	-
9	Docetaxel + trastuzumab + pertuzumab	PR	-78%	6.9 mo ¶	-	-	-	-
10	Docetaxel + trastuzumab + pertuzumab	SD	+1%	5.6 mo	T-DM1	PD	+34%	1.8 mo
11	Docetaxel + trastuzumab + pertuzumab	PD	+38%	1.8 mo	-	-	-	-
12	Docetaxel + trastuzumab + pertuzumab	PR	-68%	6.7 mo ¶	-	-	-	-
13	Docetaxel + trastuzumab + pertuzumab	SD	-2%	Ongoing at 5.5 mo	-	-	-	-

## Post-op T-DM1 in HER-2+ Salivary Gland Carcinomas

 The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT04620187

[Recruitment Status](#) ⓘ : Recruiting

[First Posted](#) ⓘ : November 6, 2020

[Last Update Posted](#) ⓘ : December 28, 2021

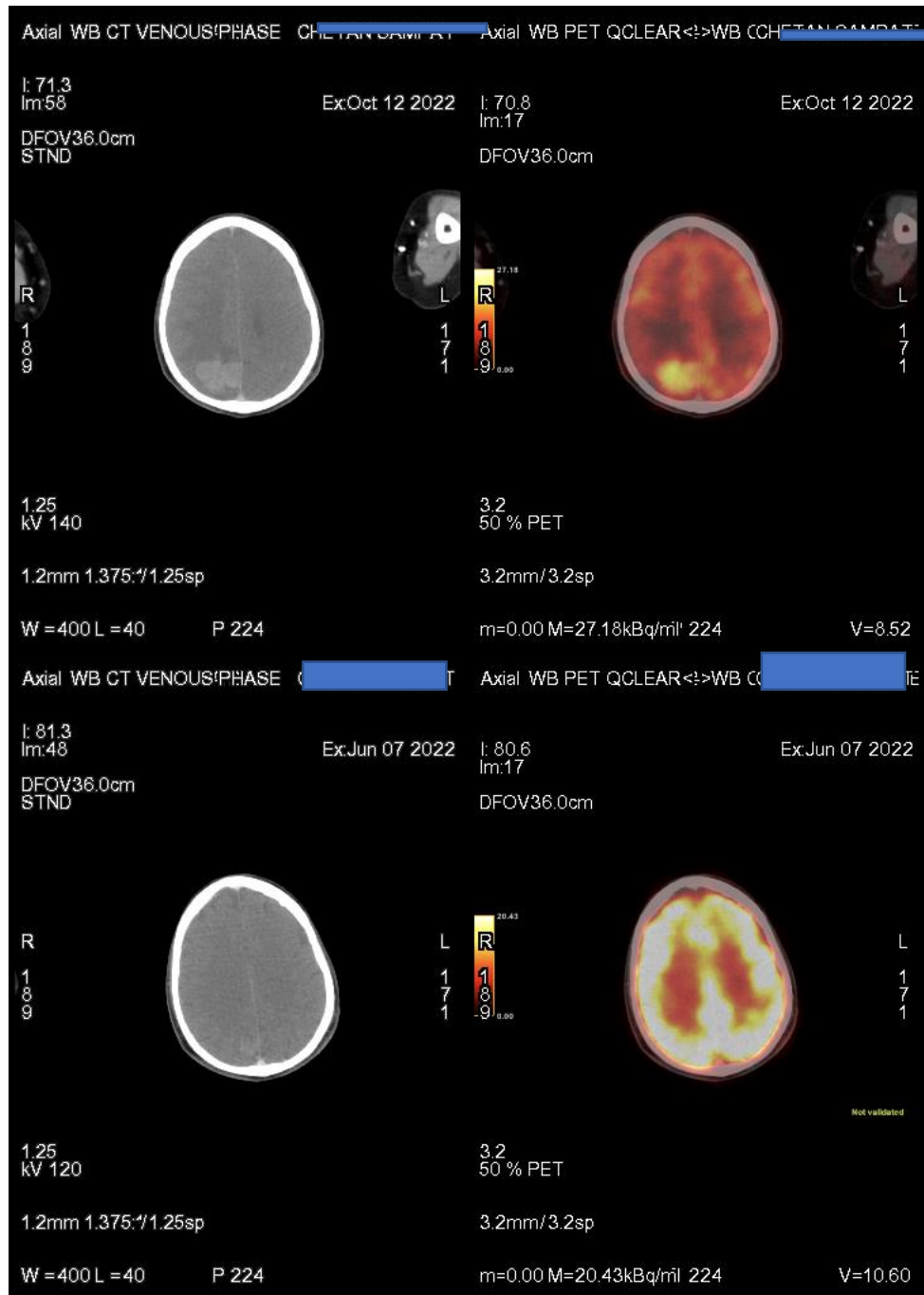
See [Contacts and Locations](#)

### Sponsor:

Dana-Farber Cancer Institute

Oct 2022: Imbalace  
MRI : Brain SOL  
PET: Oligoprogression

Sx  
WBRT



# Conclusion

- Targeting Her-2 Neu in Salivary gland tumors
  - Efficacious
  - Limited adverse events
  - We need to do this marker
- Responses are high
  - Neoadjuvant
- Adjuvant- Wait for results