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Summary of ESMO 2017

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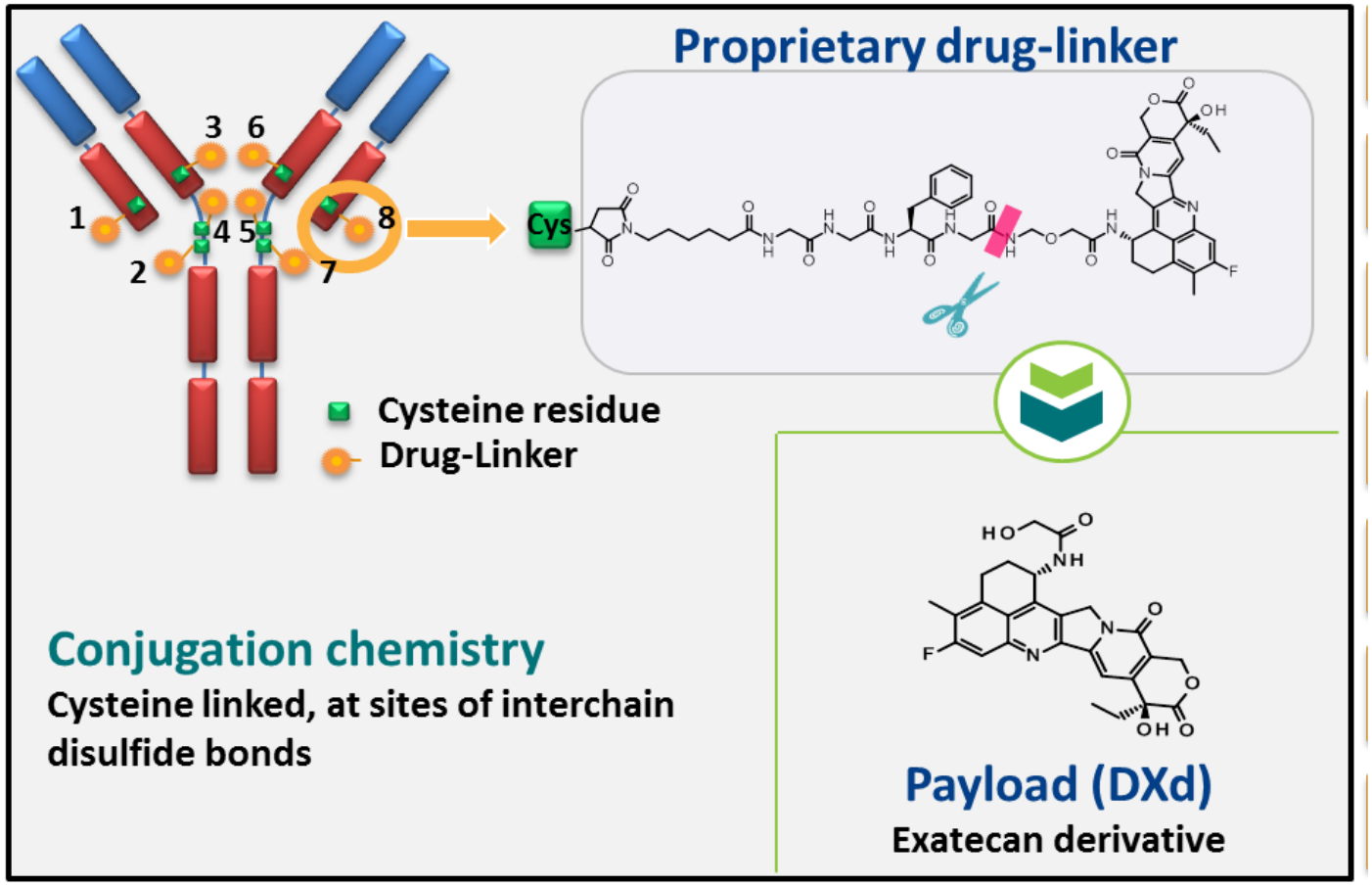
Today's Contents

- DS-8201's ESMO presentation
- DS-8201's other updates
- Other presentation at ESMO
  - DS-1205, result of non-clinical study

DS-8201's ESMO presentation

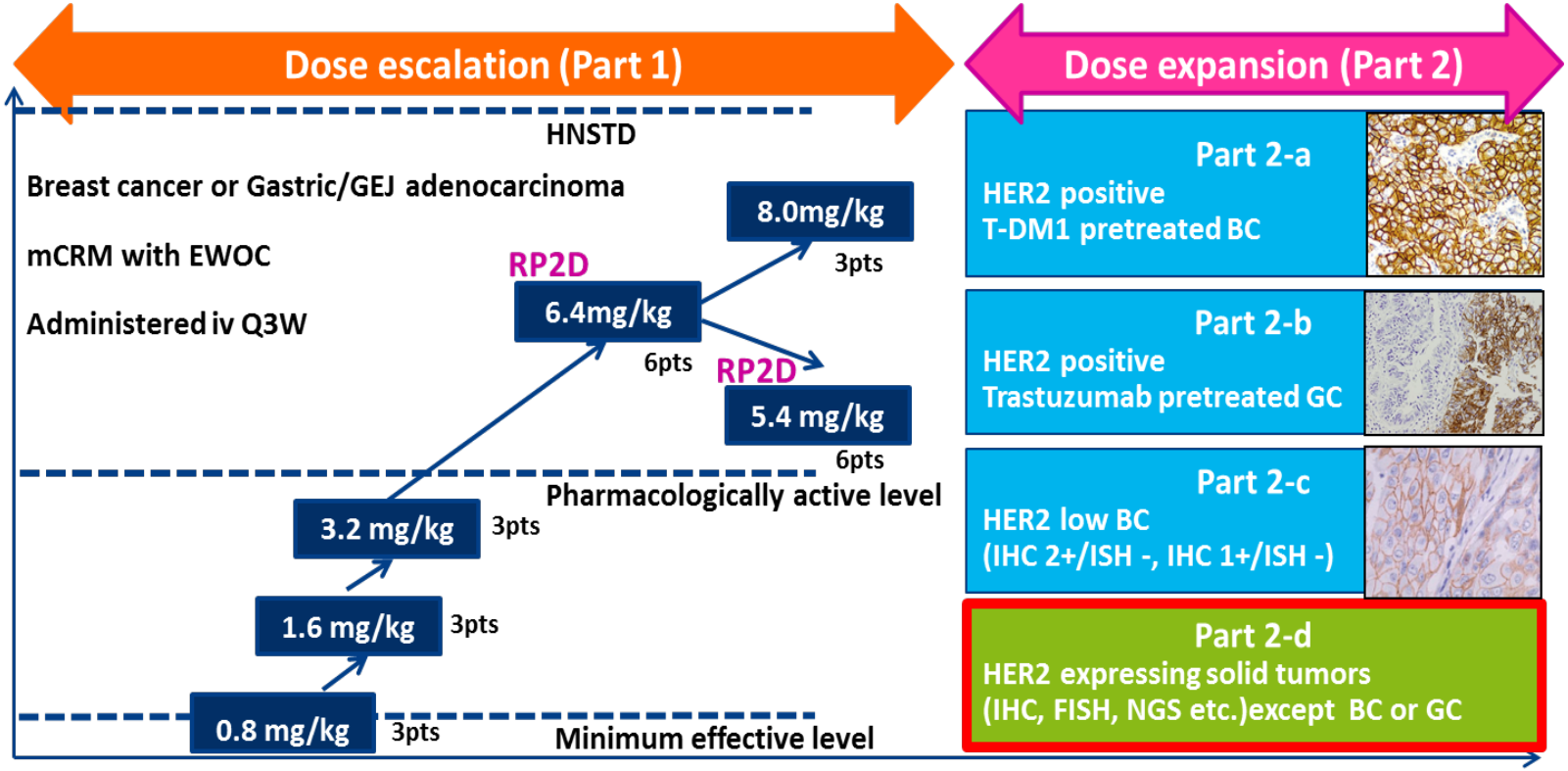
DS-8201a structure and comparison with T-DM1



	DS-8201a	T-DM1
Antibody	**Anti-HER2 Ab**	Trastuzumab
MOA	**Topoisomerase I Bystander effect**	Tubulin
Drug-to-antibody ratio	**7-8**	3.5

Multi-national first in human study design

- Results of HER2 expressing solid tumor other than breast cancer (BC) and gastric cancer (GC) in the phase 1 study were presented.
  (BC and GC results were presented at ASCO 2017)



Patient demographics (Part 2d)

Patient characteristic	Part2d (N=25)	
Age, median (range)	60.0	(44-72)
ECOG Performance Status* 0	12	(48.0%)
1	13	(52.0%)
Next generation sequencing** (5 Oncomine / 2 MSK IMPACT / SureSelect)	8	(32.0%)
Number of prior regimens, median (range)	3	(0-10)
Tumor Type†	**Part2d (N=25)**	
Colorectal	11	(44.0%)
NSCLC	6	(24.0%)
Salivary	4	(16.0%)
Others†	4	(16.0%)

† 2 Paget's disease, 1 Cholangiocarcinoma, 1 Esophageal cancer

*Eastern Cooperative Oncology Group Performance Status
0: Normal activity. Fully active, able to carry on all pre-disease performance without restriction.
1: Symptoms, but ambulatory. Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.

**One of methods to confirm HER2 status

Patient HER2 status

Herceptest ‡

		Part2d(N=25)
IHC status	0	3 (12.0%)
	1+	3 (12.0%)
	2+	2 (8.0%)
	3+	12 (48.0%)
	Unknown	1 (4.0%)
	Not examined	4 (16.0%)

‡Herceptest Scoring Criteria (CAP/ASCO 2013)

3+: Uniform intense complete membrane staining in >10% of invasive tumor cells

2+: Incomplete membrane staining that is weak to moderate in >10% of cells, or intense complete membrane staining in ≤10% of invasive tumor cells

1+: Faint, incomplete membrane staining in >10% of invasive tumor cells

0: No staining is observed in invasive tumor cells or faint incomplete membrane staining in ≤10% of cells

Safety – Summary

Category	ALL n (%)
Grade ≥3	70 (41.7)
Serious AEs	21 (12.5)
AEs leading to discontinuation	13 (7.0)
AEs with outcome of death*	1 (0.5)
Drug-related AE's with outcome of death	0 (0.0)

*Mechanical Ileus

DS-8201's ESMO presentation

Safety – TEAE, any grade, >20%

Preferred Term Part1 +Part2 Total(N=168)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	All (%)
Hematologic					
Anaemia	3.6	11.9	13.1	1.2	29.8
Platelet count decreased	11.9	7.7	6.5	3.0	29.2
Neutrophil count decreased	1.2	7.7	13.7	2.4	25.0
White blood cell count decreased	1.2	10.1	11.3	1.8	24.4
Gastrointestinal disorders					
Nausea	51.8	13.1	2.4	0.0	67.3
Decreased appetite	34.5	17.9	3.6	0.0	56.0
Vomiting	28.0	4.2	1.2	0.0	33.3
Diarrhoea	19.6	4.8	1.2	0.0	25.6
Constipation	20.8	3.0	0.6	0.0	24.4
Others					
Alopecia	20.8	5.4	0.0	0.0	26.2
Malaise	16.7	4.8	0.6	0.0	22.6

No dose-limiting toxicity (DLT) was observed and no grade 5 adverse event was observed. Low incidence of grade 4 adverse events.

DS-8201's ESMO presentation
Efficacy – Confirmed overall response rate (6.4mg/kg)

	ORR N (%) ‡	DCR N (%)
Part2d overall†	**7/22 (31.8)**	**18/22 (81.8)**
Colorectal Cancer	**2/10 (20.0)**	**8/10 (80.0)**
NSCLC	**1/5 (20.0)**	**3/5 (60.0)**
Salivary Cancer	**3/4 (75.0)**	**4/4 (100.0)**
Others §	**1/3(33.3)**	**3/3 (100.0)**

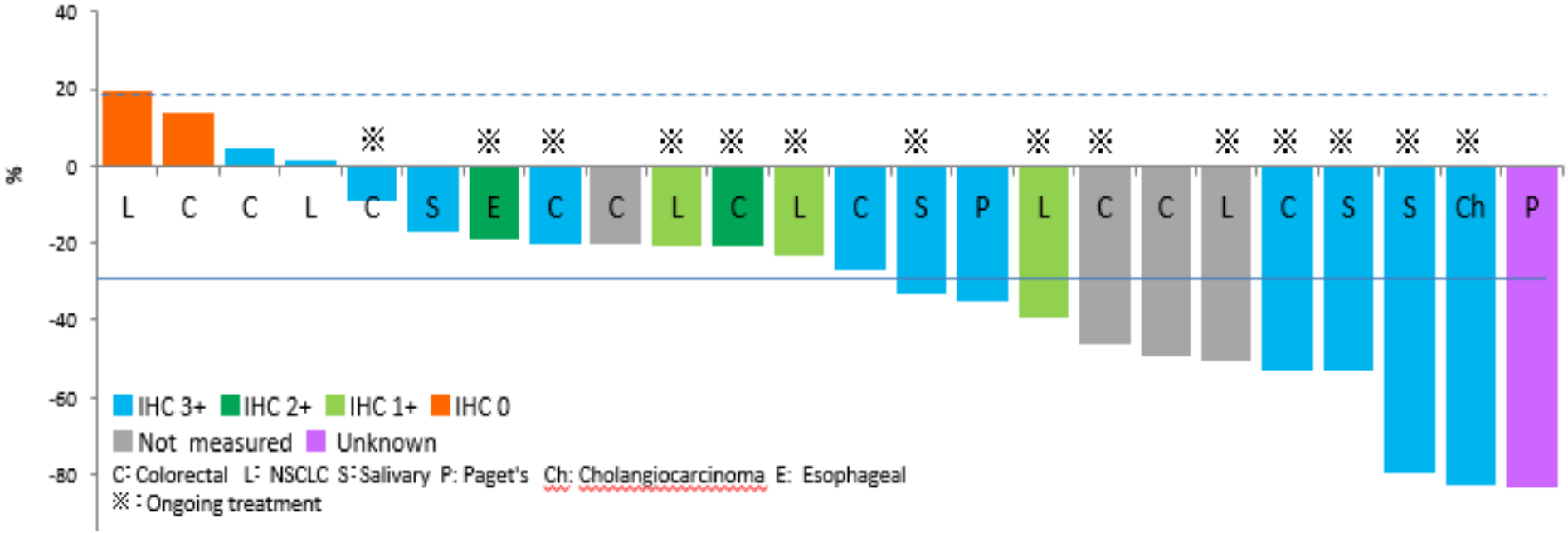
† 3 of 25 patients in 2d were enrolled, but have <2 post-baseline scans and therefore cannot be evaluated for confirmed response.

‡ 1 Colorectal Cancer and 1 Lung Cancer were evaluated once for PR-in (ongoing).

§ Others include Paget's Disease, Cholangiocarcinoma and Esophageal Cancer.

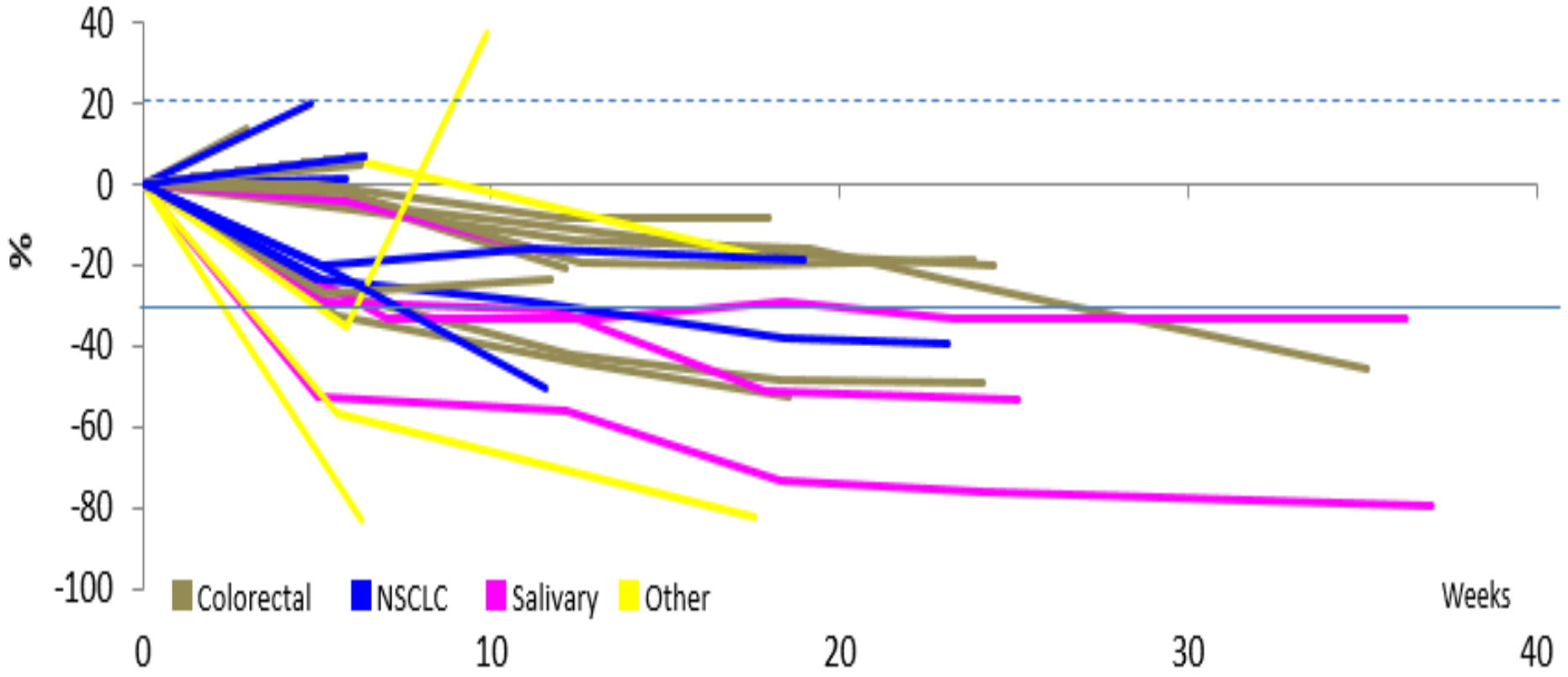
Results are interim and there are some on-going patients which PRs (partial responses) have not yet achieved.
Once duration of responses are confirmed in those patients and PRs are achieved, ORR may be increased in the future.

DS-8201's ESMO presentation
Efficacy – Tumor size: Maximum % change from baseline for Part 2d



Tumor shrinkages were observed in most of patients
(tumor shrinkage is larger when the bar goes lower and lower)

DS-8201's ESMO presentation
Efficacy – Tumor size: % Change from baseline for Part 2d

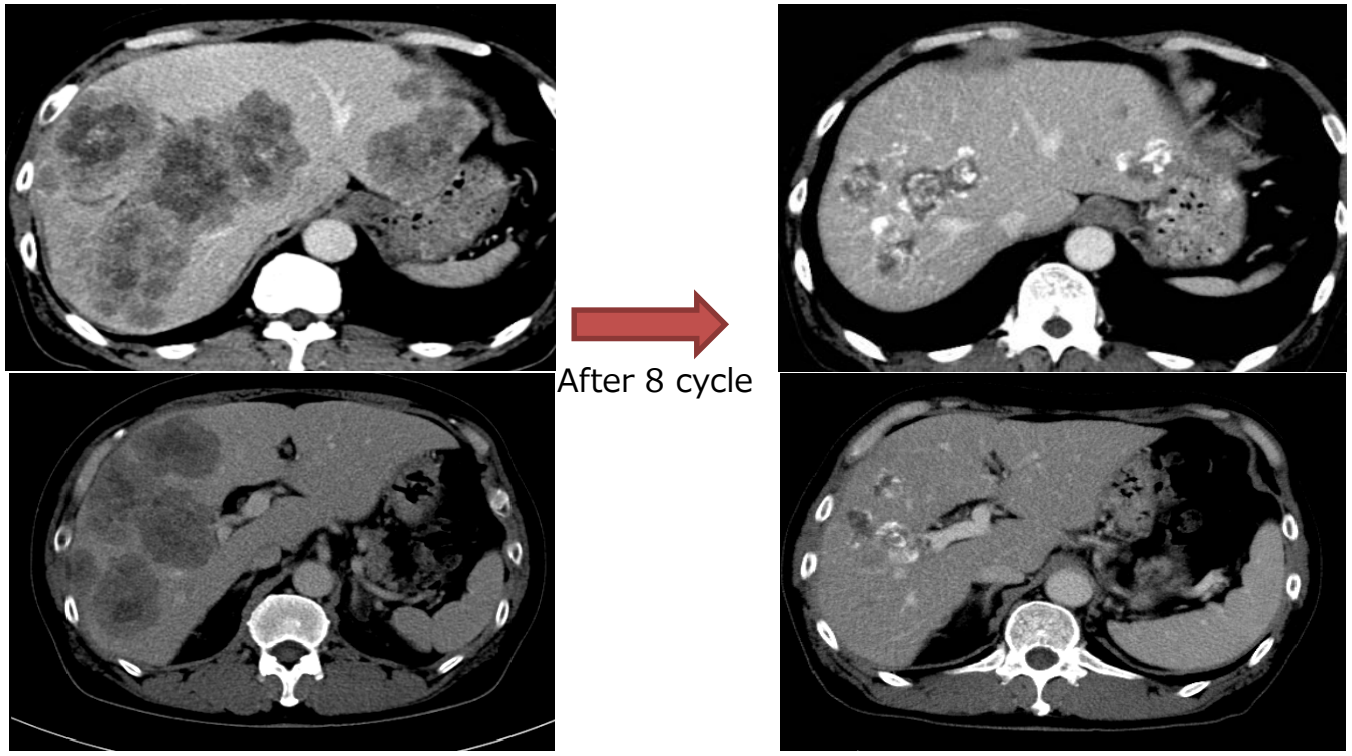


Tumor shrinkages were confirmed from early timing of treatment and tumor responses are continuing

DS-8201's ESMO presentation

CT imaging of response case

6.4mg/kg, 59 y/o Male
CRC with Liver Mets,
IHC 3+, Adenocarcinoma,
Prior FOLFIRI+BV,
CPT11+Cetuximab,
Trifluridine, Tipiracil
Hydrochloride



Day 0 Day 175

More than 30% tumor shrinkage (PR) was observed

- FOLFIRI＋BV：fluorouracil (5-FU) /leucovorin (LV) /irinotecan (IRI)+bevacizumab (BV)
- CPT11+Cetuximab：irinotecan+cetuximab
- Trifluridine, Tipiracil Hydrochloride：trifluridine and tipiracil hydrochloride (FTD)

Conclusions

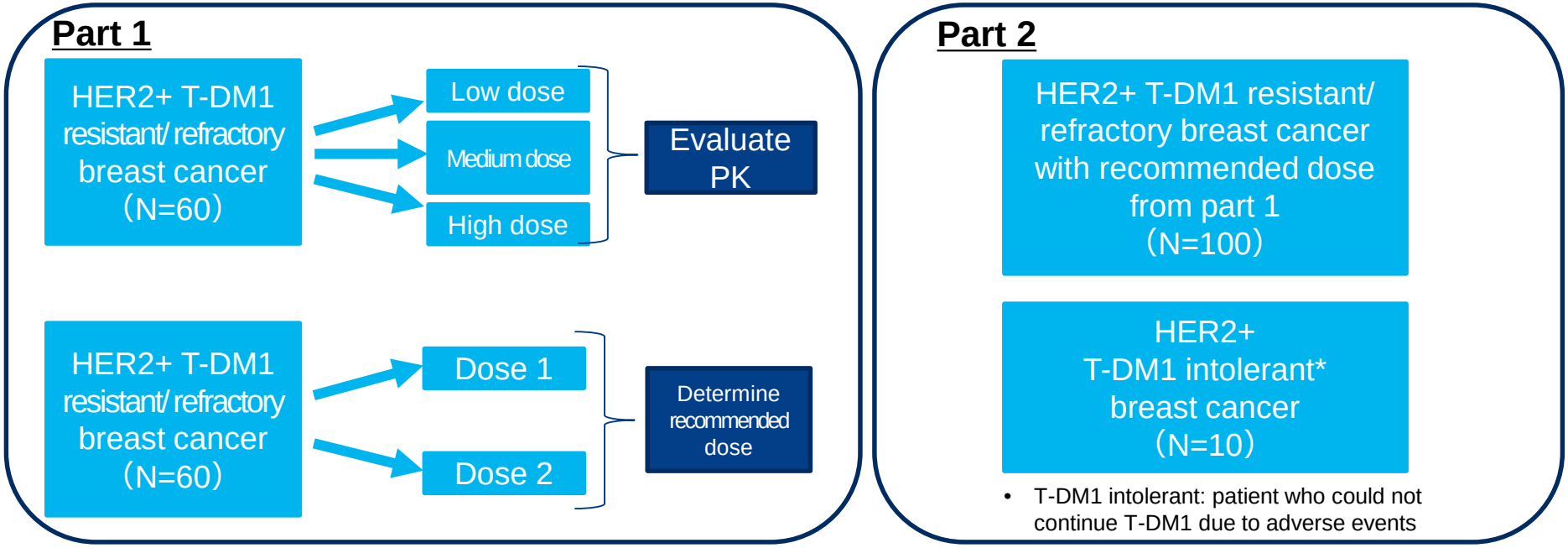
- DS-8201 was well tolerated and MTD was not reached in the dose escalation part.
- In 22 evaluable pts treated with DS-8201 for Part2d, the confirmed ORR was 31.8% and DCR was 81.8%.
- Most of the HER2 expressing solid tumors treated with DS-8201 had tumor shrinkage with the favorable safety profile.
- Based on these promising results further investigation of DS-8201 in solid tumor types beyond BC and GC is warranted.

DS-8201's other update

Breakthrough Therapy Designation

- Granted Breakthrough Therapy designation by FDA for the treatment of patients with HER2-positive, locally advanced or metastatic breast cancer who have been treated with trastuzumab and pertuzumab and have disease progression after ado-trastuzumab emtansine (T-DM1).
- Breakthrough Therapy is a process designed to expedite the development and review of medicines that may demonstrate substantial improvement over currently available treatments.
- The Breakthrough Therapy designation was granted based on the preliminary results of the ongoing phase 1 study from a subgroup analysis of HER2-positive unresectable and/or metastatic breast cancer pre-treated with trastuzumab, pertuzumab and T-DM1.

DS-8201's other update
Breast Cancer Phase 2 study (DESTINY-Breast 01 Study)



Purpose of study	Confirm efficacy of DS-8201 for HER2 positive, unresectable and/or metastatic breast cancer patients who are resistant or refractory to T-DM1
Study patients	• HER2 positive patients with T-DM1 resistant/refractory • HER2 positive patients with T-DM1 intolerant
Estimated enrollment	230 patients
Primary endpoint	ORR: Objective response rate
Study period	August 2017 ~ Aug 2019 (plan)

DS-8201's other update

Phase 1b study combination with nivolumab

Part 1: dose escalation

HER2-expressing breast cancer refractory to standard therapies / no available standard therapy

→ DS-8201 + nivolumab → Determine recommended dose

Part 2: dose expansion

HER2-expressing advanced/metastatic breast cancer

HER2-expressing urothelial (bladder) cancer previously treated with chemotherapy

→ DS-8201 + nivolumab → Evaluate the efficacy, safety and tolerability

Purpose of study	To determine recommended dose and evaluate the efficacy, safety and tolerability of DS-8201 in combination with immune checkpoint inhibitor, nivolumab
Study patients	• HER2-expressing breast cancer who are refractory to standard therapies or for which no standard therapy is available. • HER2-expressing urothelial (bladder) cancer in patients previously treated with chemotherapy.
Estimated enrollment	117 patients
Primary endpoint	ORR: Objective response rate
Study period	Start patient enrollment from Q1 2018

DS-8201: Development scope

Slide from FY2016 R&D Day

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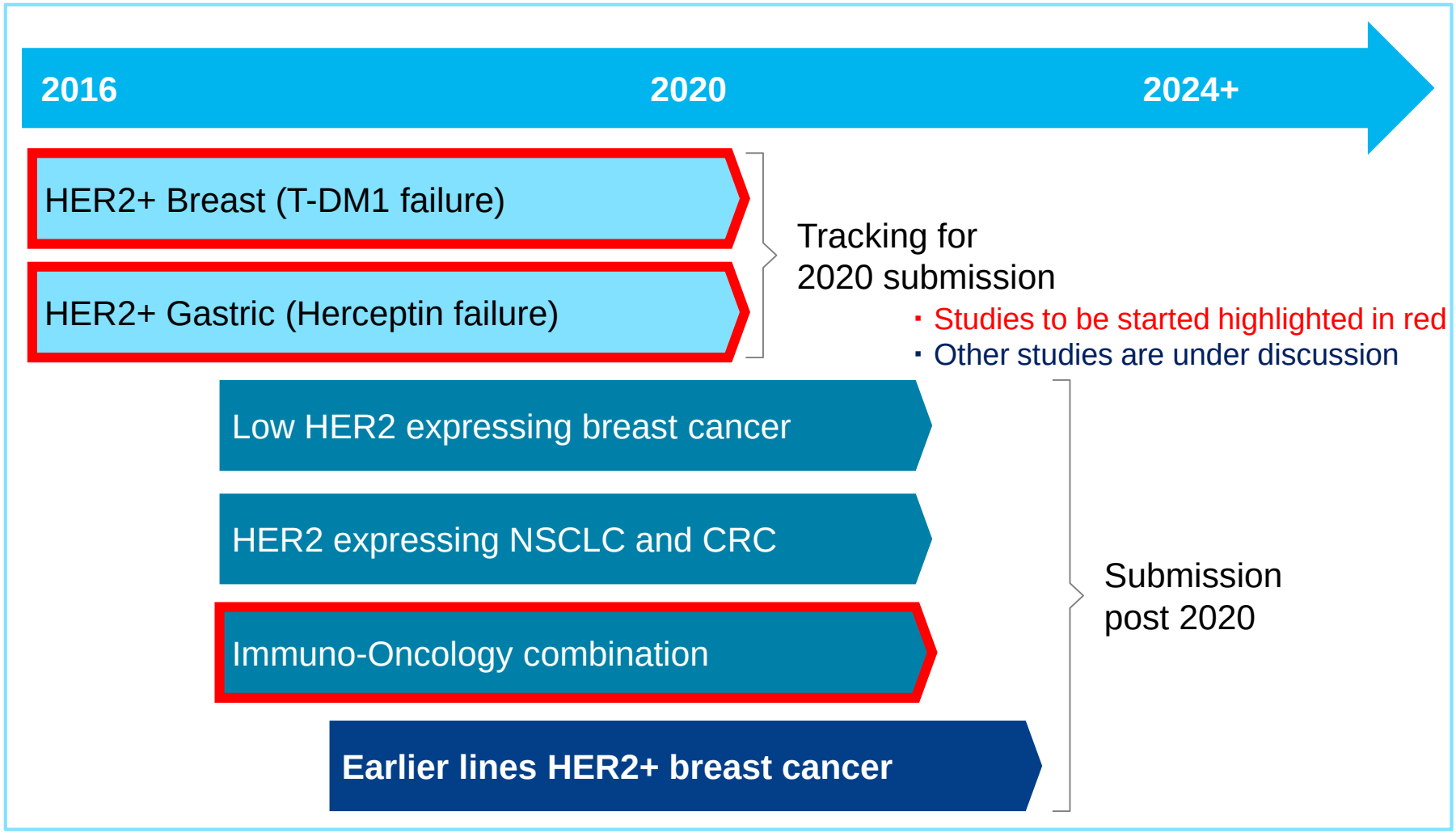
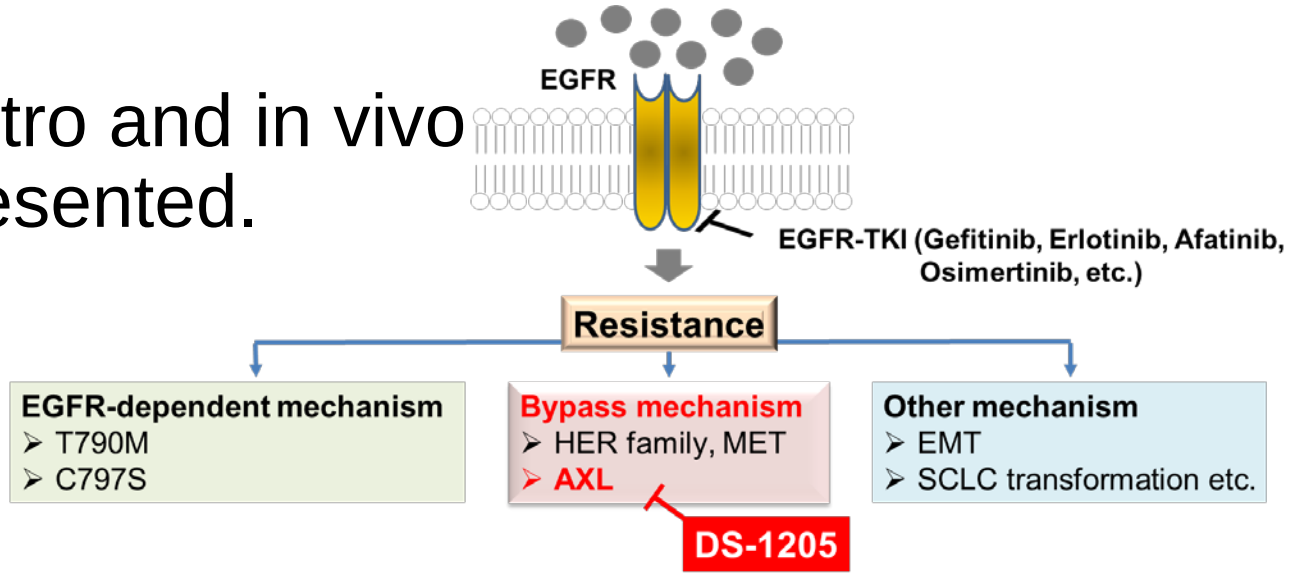


Other presentation at ESMO

DS-1205 Result of non-clinical study

- DS-1205 is an orally available small-molecule tyrosine kinase inhibitor of AXL.
- AXL up-regulation is associated with poor prognosis in several cancers.
- It has been reported that up-regulation of AXL expression is a mechanism of EGFR-TKI resistance in EGFR-mutant non-small cell lung cancer.
- Result of in vitro and in vivo study was presented.



Other presentation at ESMO

DS-1205 Result of non-clinical study

Projection only

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Osimertinib / erlorinib acquired-resistance delay effects are seen by combination with DS-1205 on xenograft model


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