R&D Conference Call

CHUGAI PHARMACEUTICAL CO., LTD.
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June 29, 2017

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Forward-Looking Statements

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the "Company"). These statements reflect the Company's current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company's businesses.

Although this presentation includes information regarding pharmaceuticals (including products under development), the information is not intended as any advertisement and/or medical advice.

Projects under Development (as of June 29, 2017)

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	Phase I	Phase II	Phase III		Filed
Oncology	**CKI27** (Japan / overseas) - solid tumors **RG7596 / polatuzumab vedotin** - NHL **RG7604 / taselisib** - solid tumors **RG7440 / ipatasertib** - solid tumors **GC33 (RG7686) / codrituzumab** - HCC★ **ERY974 (overseas)** - solid tumors **RG6078** - solid tumors		**RG1273 / Perjeta** - breast cancer (adjuvant) - gastric cancer **RG3502 / Kadcyla** - breast cancer (adjuvant) **GA101 (RG7159) / obinutuzumab** - indolent NHL **RG435 / Avastin** - RCC	**RG7446 / atezolizumab** - NSCLC (adjuvant) - SCLC - urothelial carcinoma - MIUC (adjuvant) - RCC - RCC (adjuvant) - breast cancer - ovarian cancer - prostate cancer	**RG7446 / atezolizumab** - NSCLC **AF802 (RG7853) / Alecensa** (overseas) - NSCLC [1L]

In principle, completion of first dose is regarded as the start of clinical studies in each phase.

NHL: non-Hodgkin's lymphoma
HCC: hepatocellular carcinoma
NSCLC: non-small cell lung cancer
SCLC: small cell lung cancer
MIUC: muscle invasive urothelial carcinoma
RCC: renal cell carcinoma

Letters in orange: in-house projects
★: Multinational study managed by Chugai

ASCO2017
Key Presentations Featuring Chugai Projects

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Alecensa® (alectinib)

- Alectinib versus crizotinib in treatment-naïve advanced *ALK*-positive non-small cell lung cancer: Primary results of the global phase III ALEX study [Abstract #LBA9008 (oral)]
- Updated efficacy and safety of the J-ALEX study comparing alectinib with crizotinib in ALK-inhibitor naïve ALK fusion positive non-small cell lung cancer study [Abstract #9064 (poster)]

Perjeta® (pertuzumab)

- APHINITY trial (BIG 4-11): A randomized comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with HER2-positive early breast cancer [Abstract #LBA500 (oral)]

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Atezolizumab

1. Non-Small Cell Lung Cancer (NSCLC)
   - Impact of atezolizumab treatment beyond disease progression (TBP) in advanced NSCLC: Results from the randomized phase III OAK study [Abstract #9001 (oral)]
   - Atezolizumab plus platinum-based chemotherapy (chemo) in non-small cell lung cancer: Update from a phase 1b study [Abstract #9092 (poster)]
2. Renal Cell Carcinoma
   - IMmotion 150: A phase II trial in untreated metastatic renal cell carcinoma patients of atezolizumab and bevacizumab vs and following atezo or sunitinib [Abstract #4505 (oral)]

ASCO2017
Key Presentations Featuring Chugai Projects

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Ipatasertib

- LOTUS: A double-blind placebo-controlled randomized phase II trial of first-line ipatasertib + paclitaxel for metastatic triple-negative breast cancer (TNBC) [Abstract #1009 (poster discussion)]

ERY974

- A phase I dose escalation and cohort expansion study of ERY974, a T-cell redirecting bispecific antibody against Glypican 3 in patients with advanced solid tumors [Abstract #TPS3112 (poster)]

CKI27

- Results from the biomarker-driven basket trial of RO5126766 (CH5126766), a potent RAF/MEK inhibitor, in RAS- or RAF- mutated malignancies including multiple myeloma [Abstract #2506 (oral)]

Alecensa
ALEX Study: Study Design

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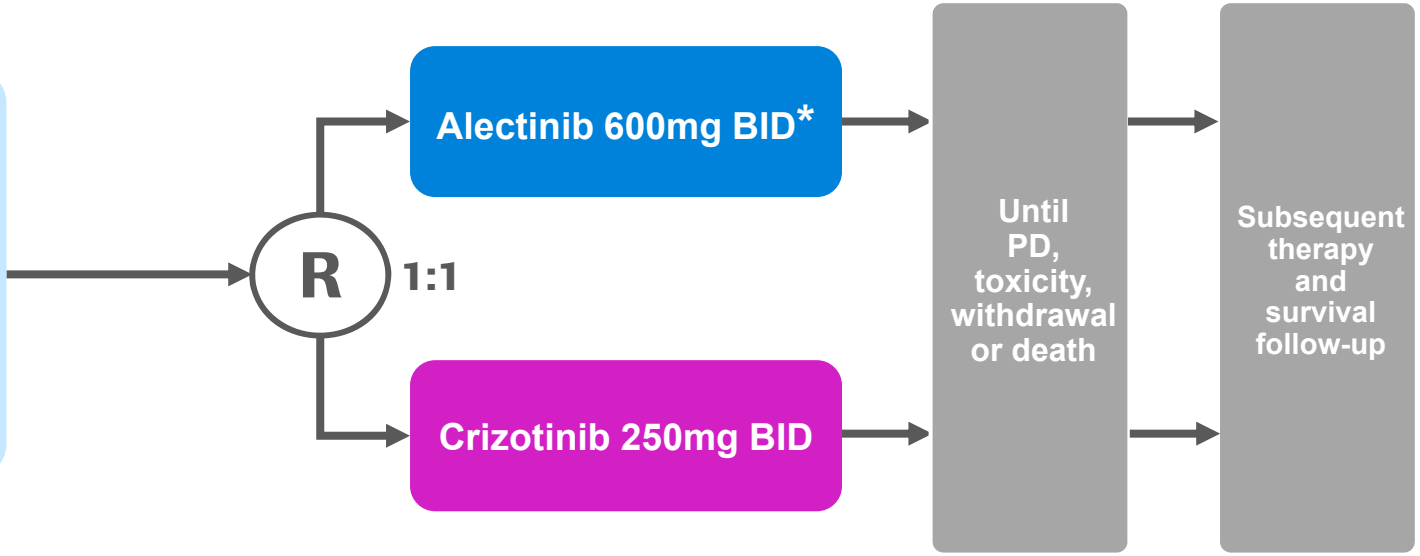
- Stage IIIB/IV NSCLC
- *ALK*+ disease according to IHC test
- Treatment naïve
- ECOG PS 0–2

(n=303)



Stratification factors

- ECOG PS (0/1 vs 2)
- Ethnicity (Asian vs non-Asian)
- CNS metastases at baseline (presence vs absence)

Primary endpoint

- PFS (investigator assessed)

Secondary endpoints

- PFS by IRC
- Time to CNS progression
- ORR
- DoR
- OS
- CNS ORR
- CNS DoR
- QoL
- Safety

Modified from Shaw A. *et al,* ASCO 2017; ECOG PS=Eastern Cooperative Oncology Group Performance Status; BID=twice daily dosing; CNS=central nervous system; PFS=progression free survival; IRC=independent review committee; ORR=overall response rate; DoR=duration of response

* Approved dosage of Alectinib in Japan is 300mg BID

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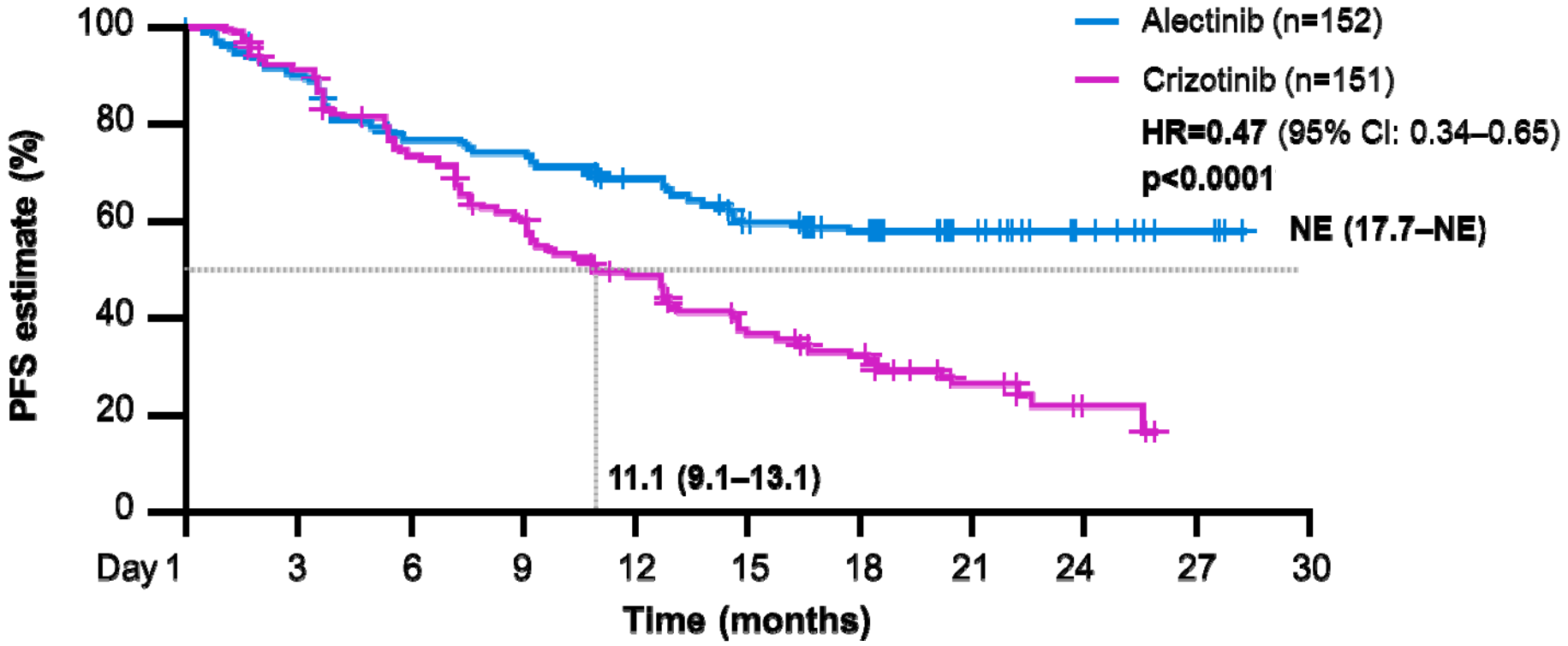
ALEX Study: Efficacy

Primary endpoint: Investigator-assessed PFS



Modified from Shaw A. *et al,* ASCO 2017; HR=hazard ratio; NE=not estimable

* Approved dosage of Alectinib in Japan is 300mg BID

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ALEX Study: Efficacy

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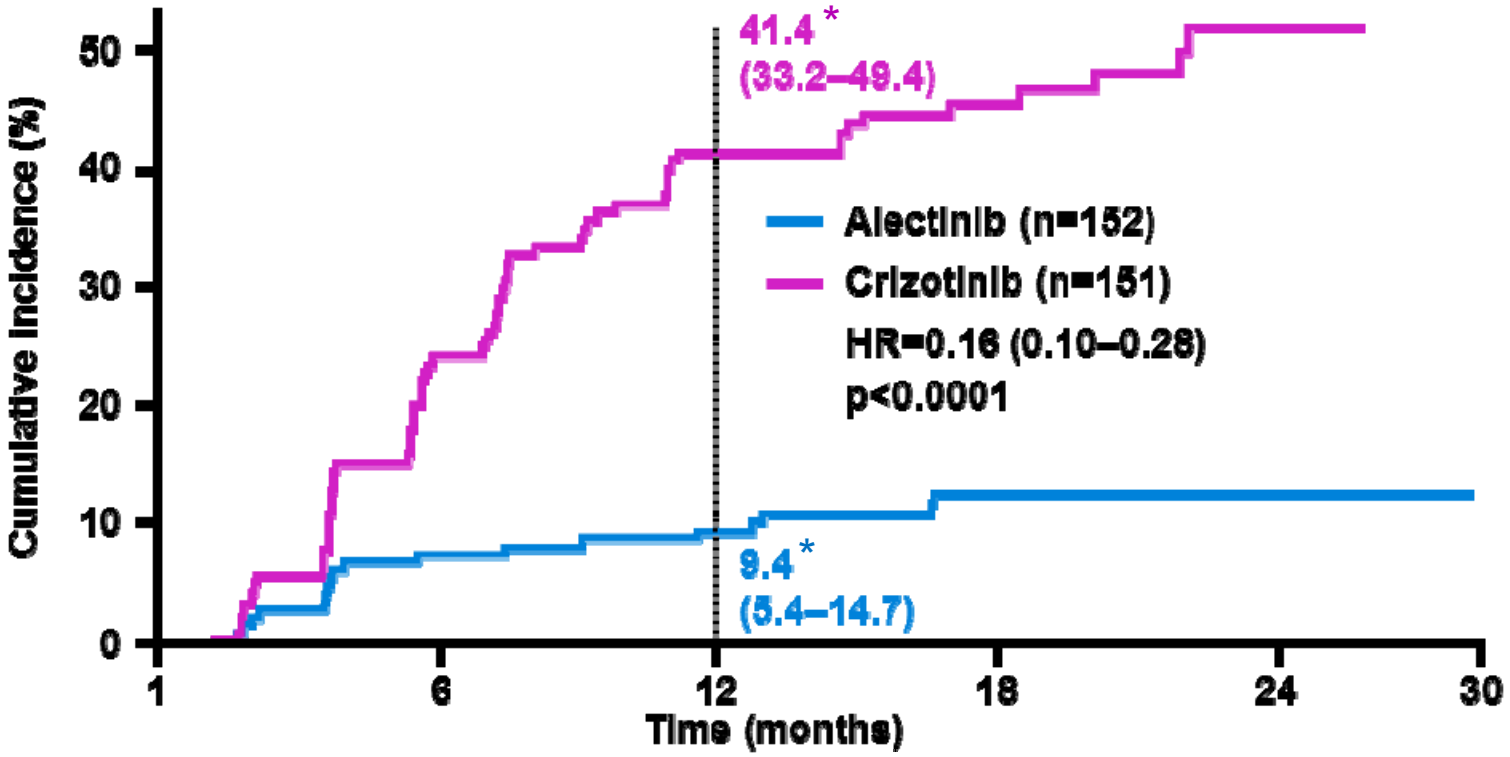
Secondary endpoint: Time to CNS progression (by IRC, ITT)



Modified from Shaw A. *et al,* ASCO 2017; CNS=central nervous system; IRC=independent review committee; ITT=intent to treat;
*=12-month cumulative incidence rate

* Approved dosage of Alectinib in Japan is 300mg BID

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ALEX Study: Safety

Adverse events, ≥10% between treatment arms

	Crizotinib (N=151)		Alectinib (N=152)	
N (%)	Any grade	Grade 3–5	Any grade	Grade 3–5
Nausea	72 (48)	5 (3)	21 (14)	1 (1)
Diarrhea	68 (45)	3 (2)	18 (12)	0
Vomiting	58 (38)	5 (3)	11 (7)	0
Peripheral edema	42 (28)	1 (1)	26 (17)	0
Dysgeusia	29 (19)	0	4 (3)	0
ALT increased	45 (30)	22 (15)	23 (15)	7 (5)
AST increased	37 (25)	16 (11)	21 (14)	8 (5)
Visual impairment	18 (12)	0	2 (1)	0
Blood bilirubin increased	2 (1)	0	23 (15)	3 (2)
Myalgia	3 (2)	0	24 (16)	0
Anemia	7 (5)	1 (1)	30 (20)	7 (5)
Weight increased	0	0	15 (10)	1 (1)

Modified from Shaw A. *et al,* ASCO 2017; ALT=alanine aminotransferase; AST=aspartate transaminase

* Approved dosage of Alectinib in Japan is 300mg BID

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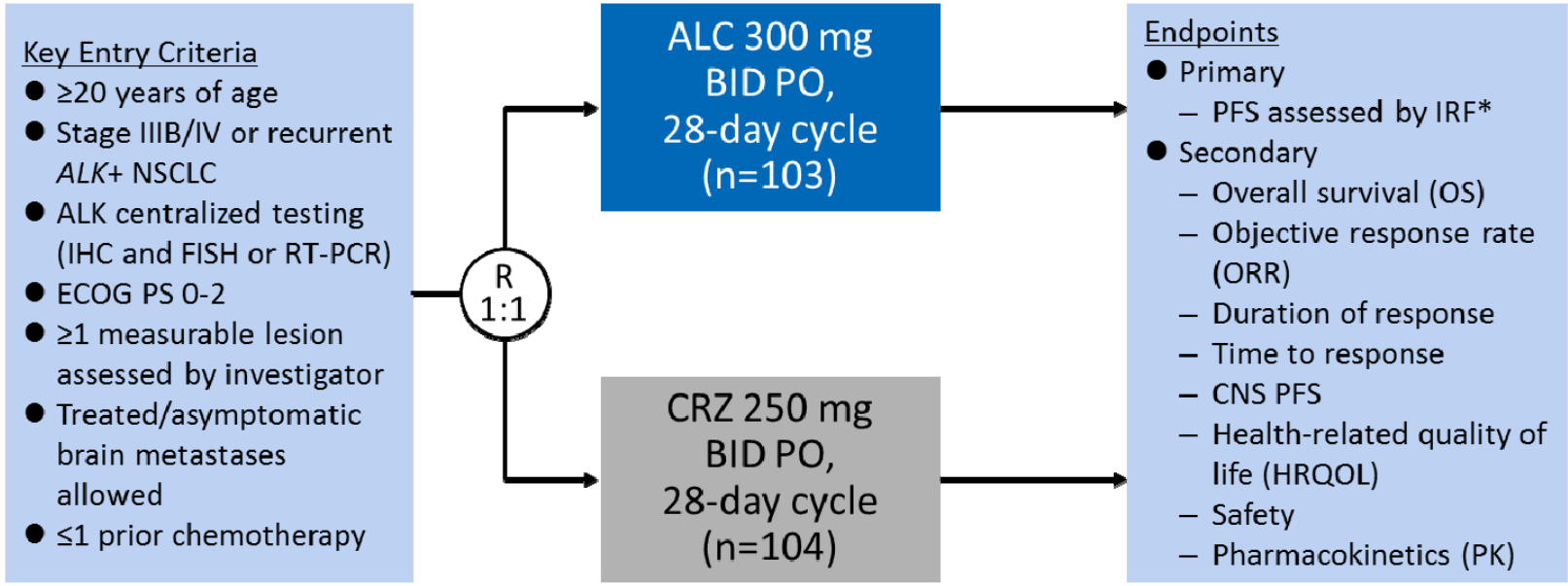
J-ALEX: Study Design

- Patients with advanced *ALK*+ NSCLC were randomized 1:1 to receive oral ALC 300 mg BID or oral CRZ 250 mg BID until disease progression or unacceptable toxicity.
- Stratification factors were ECOG PS (0/1 vs. 2), treatment line (1st vs. 2nd), and clinical stage (IIIB/IV vs. recurrent).

STUDY DESIGN



*IRF: Independent Review Facility

Modified from Takiguchi Y. *et al,* ASCO 2017; ALC=alectinib; CRZ=crizotinib; PO=by mouth

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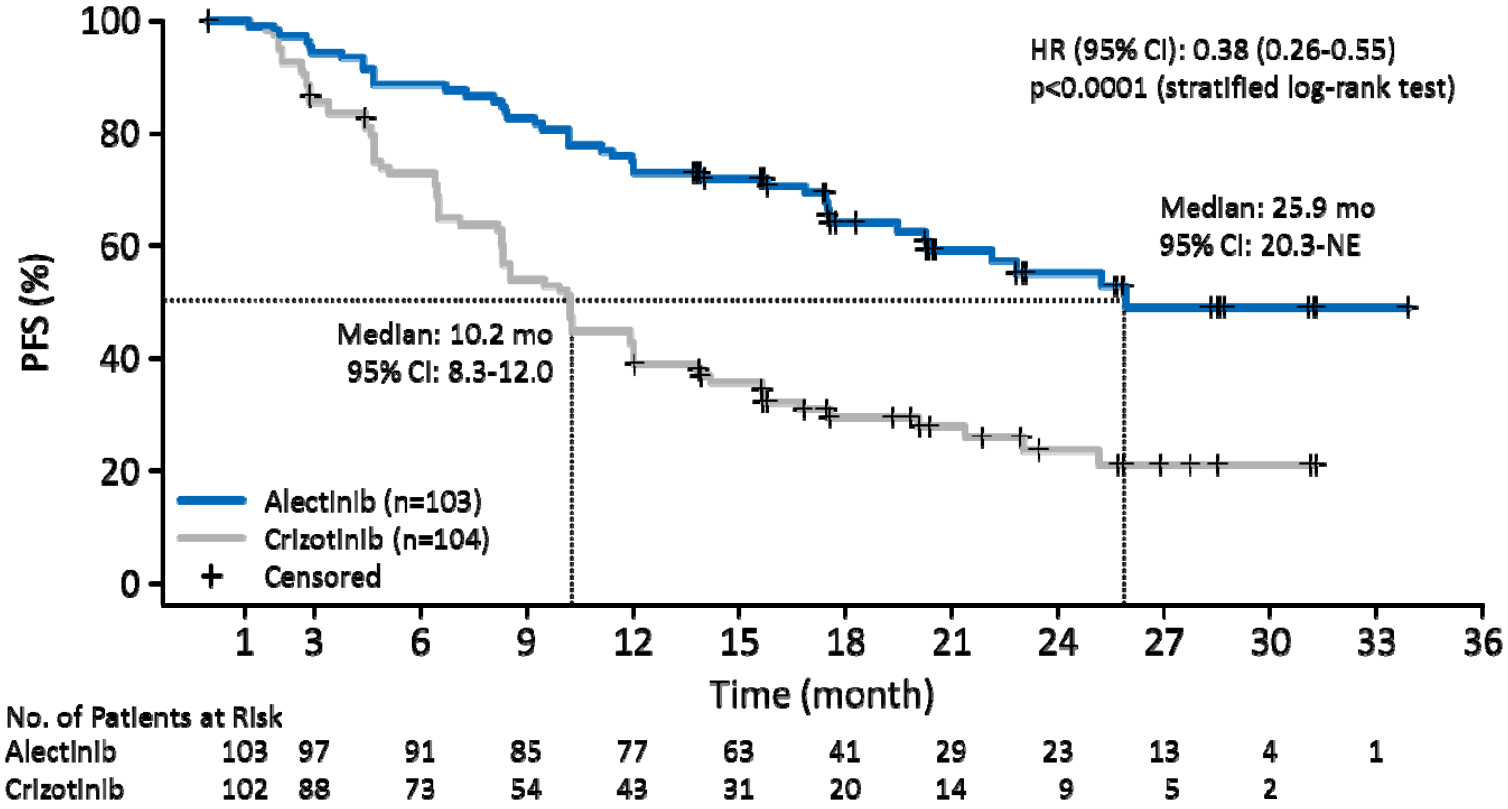
J-ALEX: Efficacy

Primary endpoint: PFS by IRF in the intent-to-treat (ITT) population



- The safety profiles were consistent with those seen in previous studies.

Modified from Takiguchi Y. *et al,* ASCO 2017

Pertuzumab
APHINITY: Study Design

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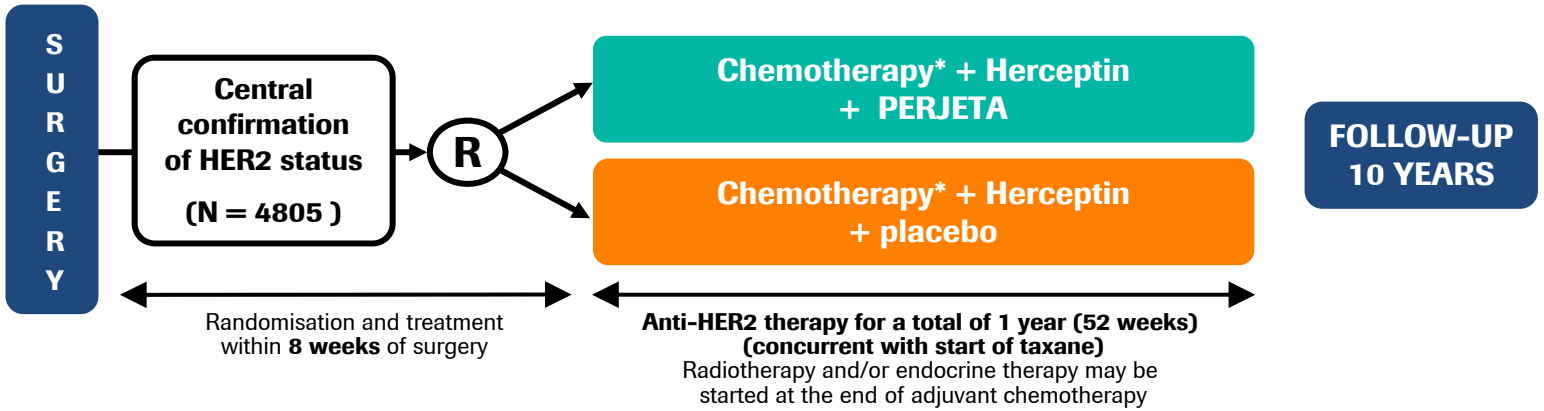
Randomized phase III study in patients with HER2-positive early breast cancer



* A limited number of standard anthracycline or non-anthracycline (TCH) regimens were allowed

Primary endpoint: IDFS (Invasive Disease-Free Survival)

Secondary endpoints: IDFS including second primary non-breast cancer, disease-free interval, OS, safety, HRQoL

Stratification factors:

- Chemo regimen
- HR status
- Nodal status
- Geographic region
- Protocol version

Modified from Minckwitz G. *et al,* ASCO 2017

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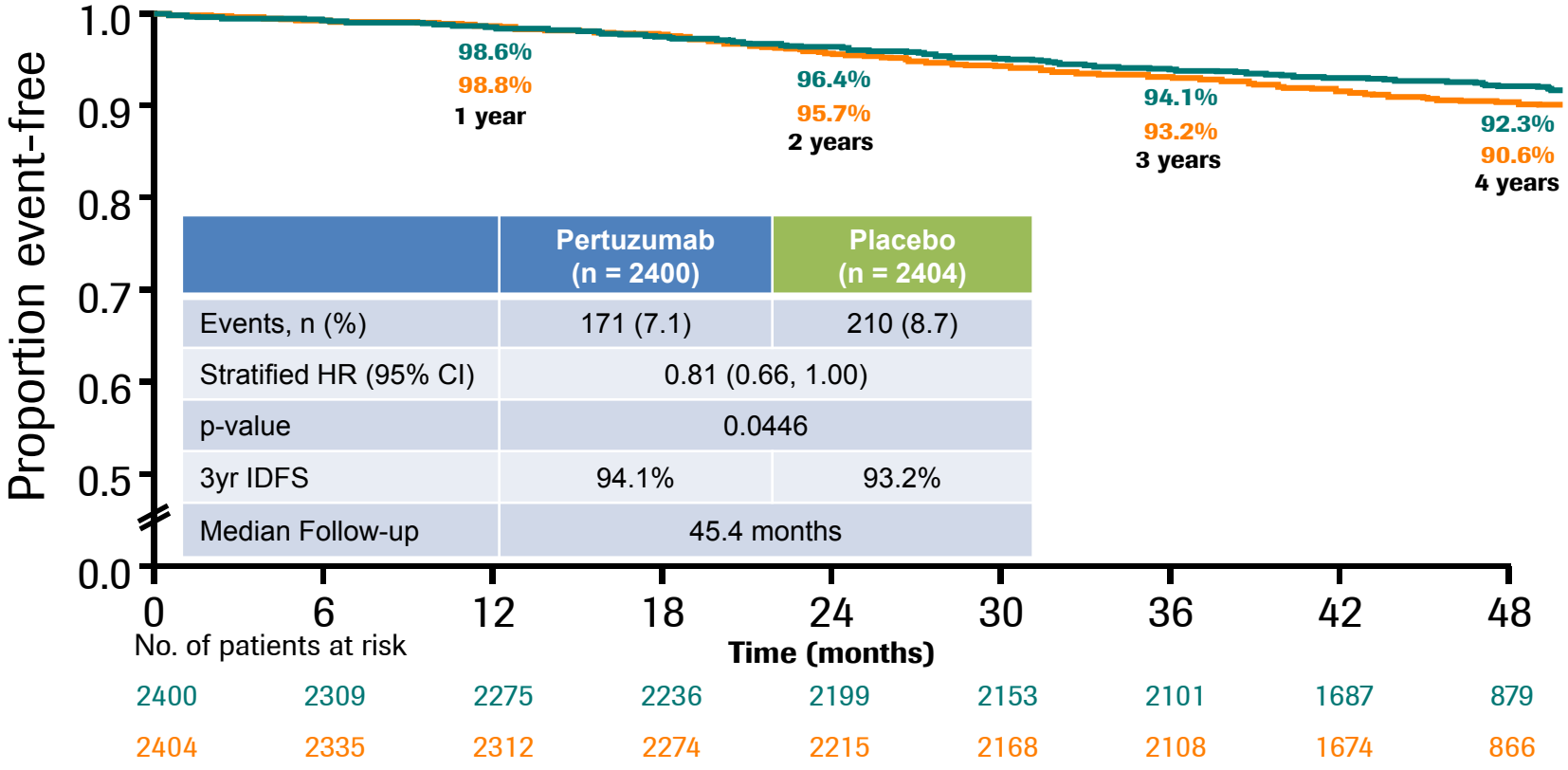
Pertuzumab
APHINITY: Primary Analysis (IDFS)



	Pertuzumab (n = 2400)	Placebo (n = 2404)
Events, n (%)	171 (7.1)	210 (8.7)
Stratified HR (95% CI)	0.81 (0.66, 1.00)	
p-value	0.0446	
3yr IDFS	94.1%	93.2%
Median Follow-up	45.4 months	

- The safety profiles were consistent with those seen in previous studies.

Modified from Minckwitz G. *et al,* ASCO 2017

Pertuzumab
APHINITY: Subgroup Analysis (Nodal Status)

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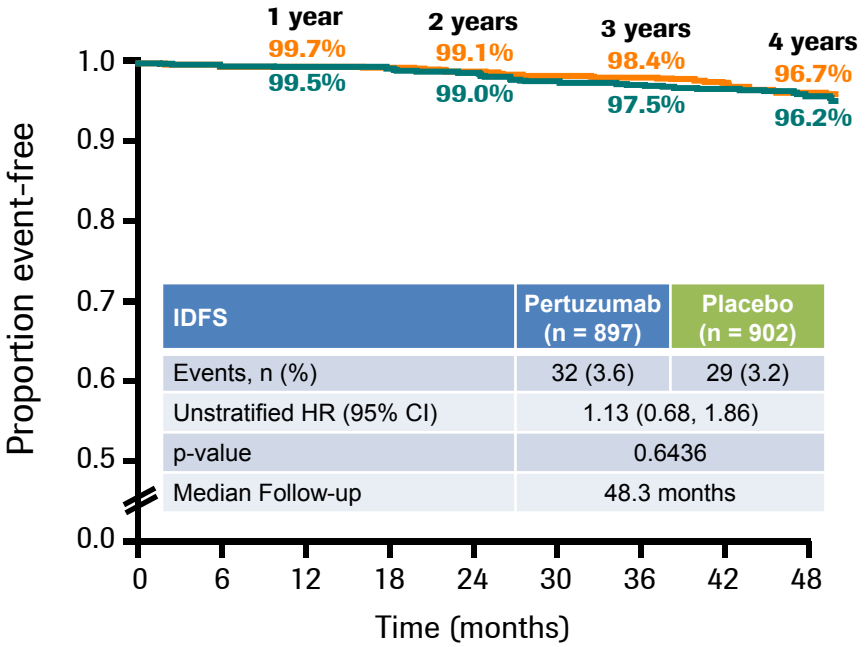
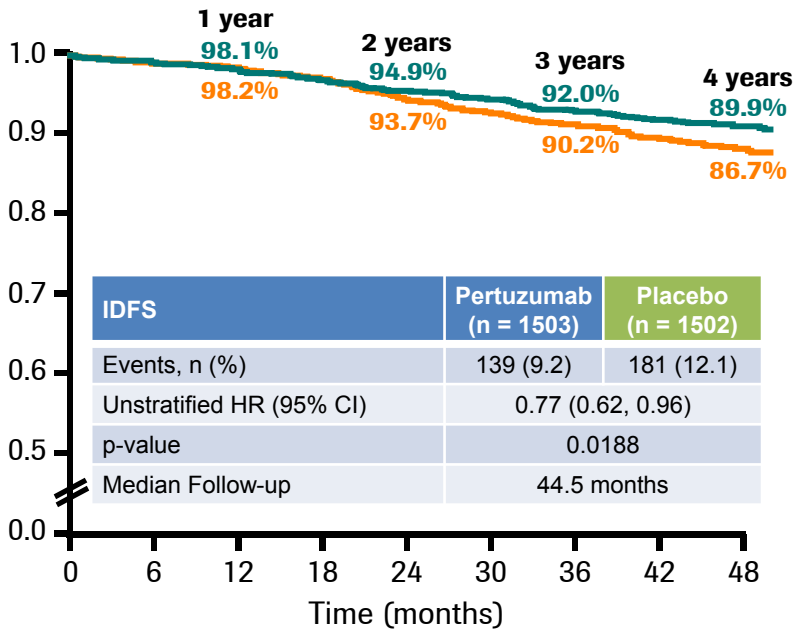
Lymph node-negative subgroup (n = 1799)



IDFS	Pertuzumab (n = 897)	Placebo (n = 902)
Events, n (%)	32 (3.6)	29 (3.2)
Unstratified HR (95% CI)	1.13 (0.68, 1.86)	
p-value	0.6436	
Median Follow-up	48.3 months	

No. of patients at risk									
	897	865	856	849	841	826	818	775	456
	902	882	873	866	856	849	844	792	461

Lymph node-positive subgroup (n = 3005)



IDFS	Pertuzumab (n = 1503)	Placebo (n = 1502)
Events, n (%)	139 (9.2)	181 (12.1)
Unstratified HR (95% CI)	0.77 (0.62, 0.96)	
p-value	0.0188	
Median Follow-up	44.5 months	

No. of patients at risk									
	1503	1444	1419	1387	1358	1327	1283	912	423
	1502	1453	1439	1408	1359	1319	1264	882	405

Modified from Minckwitz G. *et al,* ASCO 2017

Pertuzumab
APHINITY: Subgroup Analysis (HR Status)

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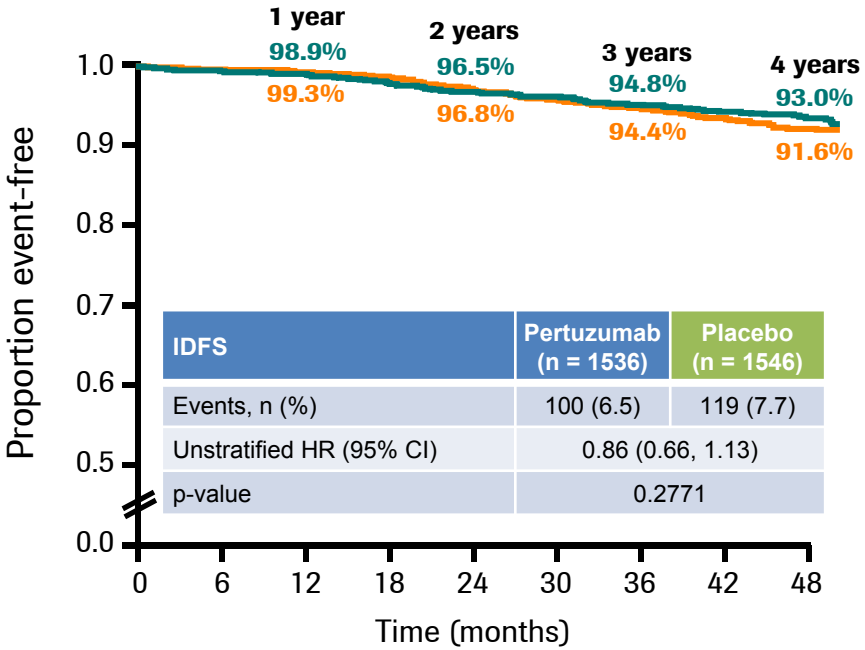
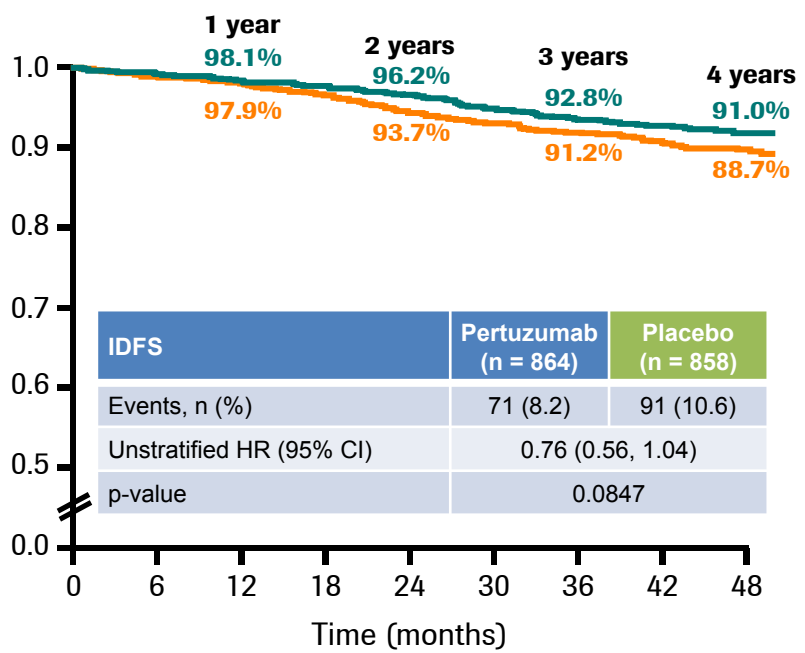
HR-positive subgroup (n = 3082)



IDFS	Pertuzumab (n = 1536)	Placebo (n = 1546)
Events, n (%)	100 (6.5)	119 (7.7)
Unstratified HR (95% CI)	0.86 (0.66, 1.13)	
p-value	0.2771	

No. of patients at risk									
Pertuzumab	1536	1473	1454	1423	1402	1379	1346	1087	565
Placebo	1546	1508	1501	1481	1444	1410	1378	1105	564

HR-negative subgroup (n = 1722)



IDFS	Pertuzumab (n = 864)	Placebo (n = 858)
Events, n (%)	71 (8.2)	91 (10.6)
Unstratified HR (95% CI)	0.76 (0.56, 1.04)	
p-value	0.0847	

No. of patients at risk									
Pertuzumab	864	836	821	813	797	774	755	600	314
Placebo	858	827	811	793	771	758	730	569	302

Modified from Minckwitz G. *et al,* ASCO 2017; HR=hormone receptor

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Ipatasertib
LOTUS: Study Design

Double-blind placebo controlled randomized phase II study

- Inoperable locally advanced/ metastatic TNBC
- No prior systemic therapy for advanced/metastatic disease (n =˜ 120)

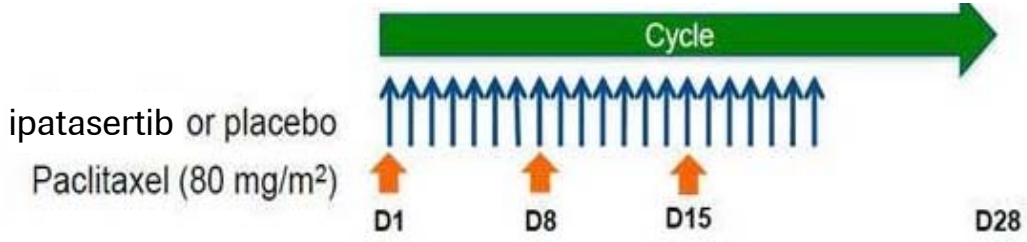
R 1:1

Paclitaxel 80 mg/m² days 1, 8 & 15 + ipatasertib 400 mg qd days 1–21 q28d

Paclitaxel 80 mg/m² days 1, 8 & 15 + placebo days 1–21 q28d

Stratification Factors

- (Neo)adjuvant chemotherapy* (yes vs no)
- Chemotherapy-free interval (≤12 vs >12 months vs no prior chemo)
- Tumor PTEN status (H-score 0 vs 1-150 vs >150, by TARGOS)



Primary Endpoints

- PFS in ITT population
- PFS in PTEN-low subgroup (by Ventana IHC)

Secondary Endpoints

- ORR, DoR and OS in all patients and PTEN-low subgroup
- PFS, ORR, DoR and OS in FMI NGS Dx+ subgroup (PI3K/Akt pathway-activated tumors)
- Safety and tolerability

Modified from Dent R. *et al,* ASCO 2017; TNBC=triple-negative breast cancer; PTEN=phosphatase and tensin homolog; FMI=Foundation Medicine, Inc.; NGS=next-generation sequencing

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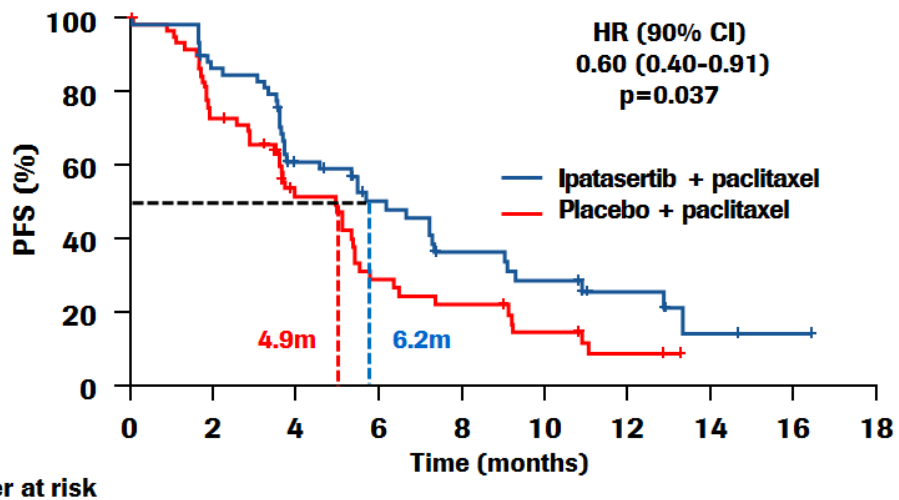
Ipatasertib
LOTUS: Efficacy (PFS)

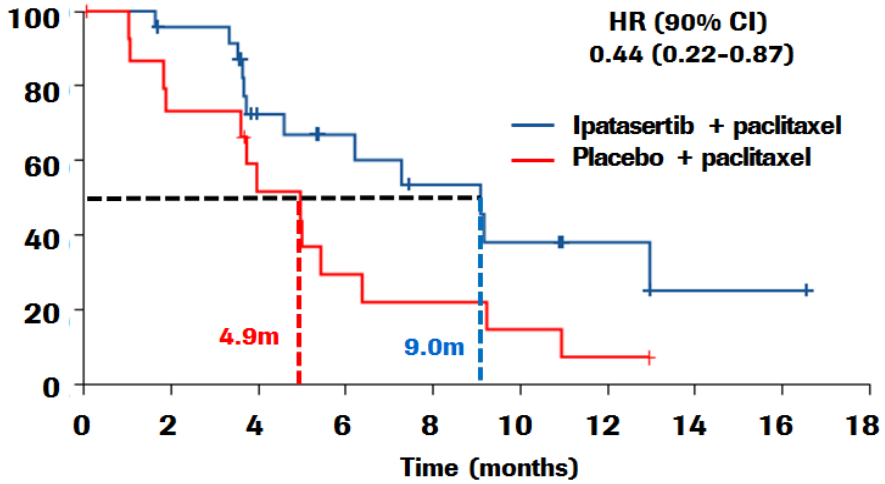
ITT population



Number at risk

Ipatasertib + pac	62	50	31	22	14	11	6	2	1
Placebo + pac	62	43	23	13	10	6	3		

PIK3CA/AKT1/PTEN-altered tumor population



	26	22	13	10	7	5	3	1	1
	16	11	7	4	3	2	1		

Modified from Dent R. *et al,* ASCO 2017

ERY974 (TRAB)

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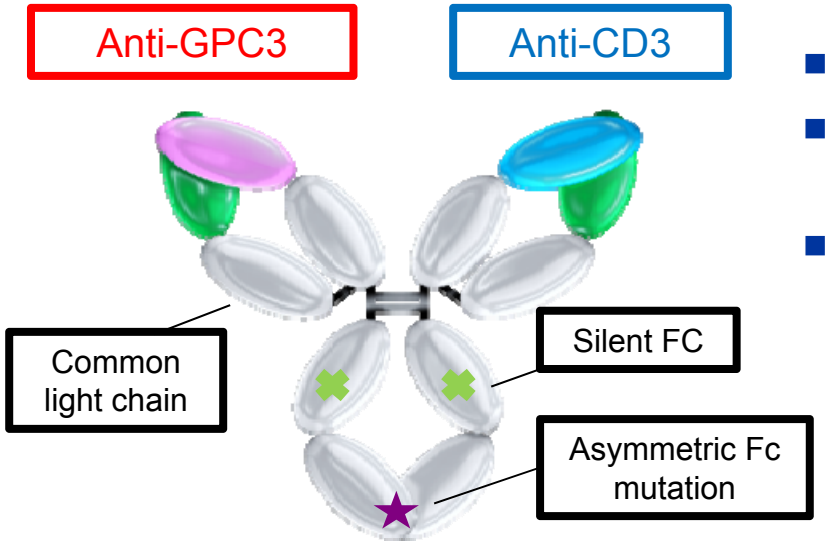

- Humanized IgG4 monoclonal antibody
- Fc region mutated to reduce non-specific cytokine release
- Plasma T1/2 is expected to be 2-5 days

Multicenter, international Phase I dose escalation and cohort expansion study

Study objectives

- Determination of dose limiting toxicities (DLTs) and establishing recommend dose (RD)
- Evaluate anti-tumor efficacy in 3 tumor type specific cohorts treated at the RD

Ongoing dose escalation cohort

- No DLT is observed
- Cytokine release syndrome with IL-6 elevation is observed
- Dose escalation is ongoing

Modified from Hashimoto K. *et al,* ASCO 2017; TRAB=T-cell redirecting antibody

Efficacy of ERY974 in Preclinical Models

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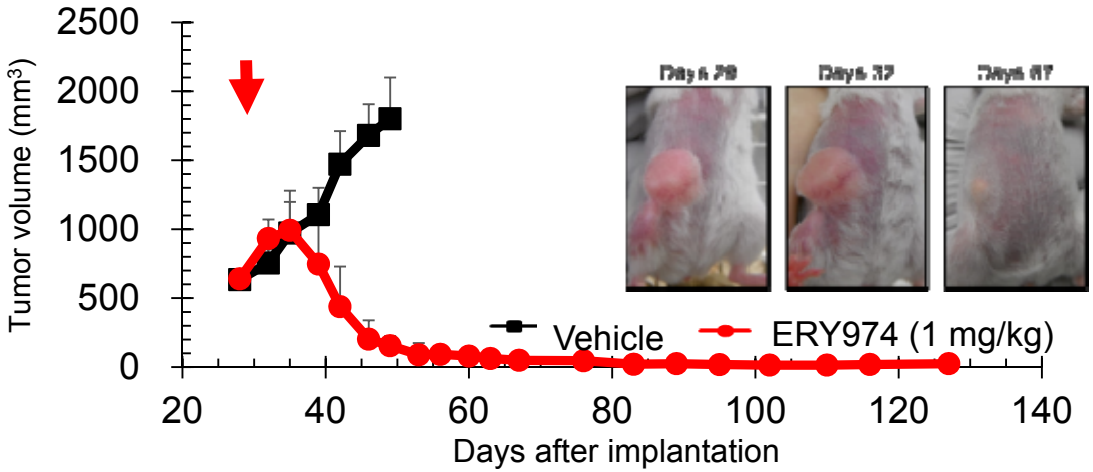
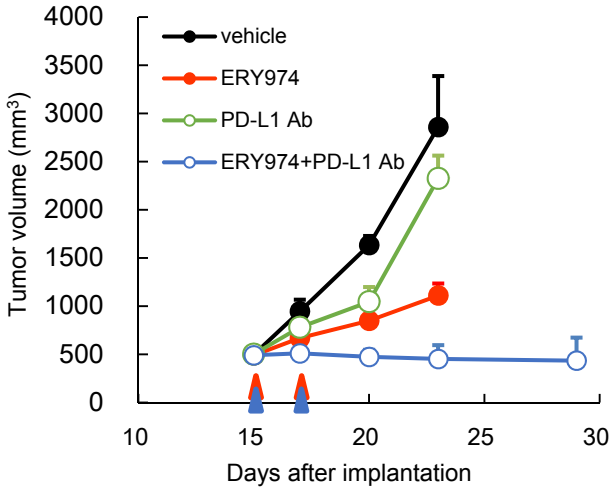
(Sano Y. et al., AACR2017)

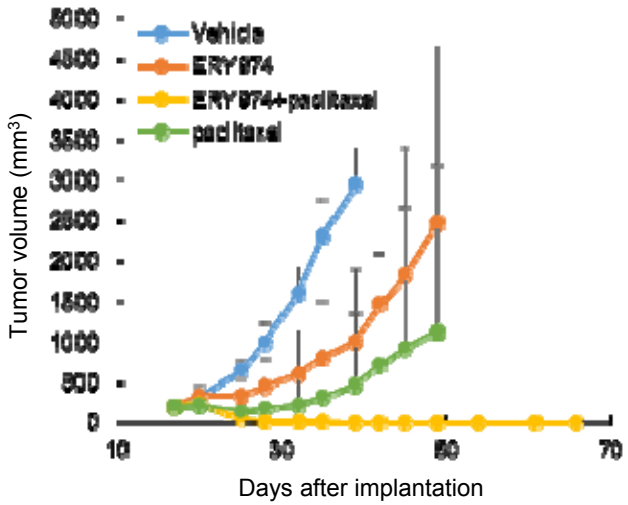
ERY974 monotherapy (KYSE70)



ERY974 + PD-L1 Ab (Hepa1-6/hGPC3)



ERY974 + paclitaxel (NCI-H446)



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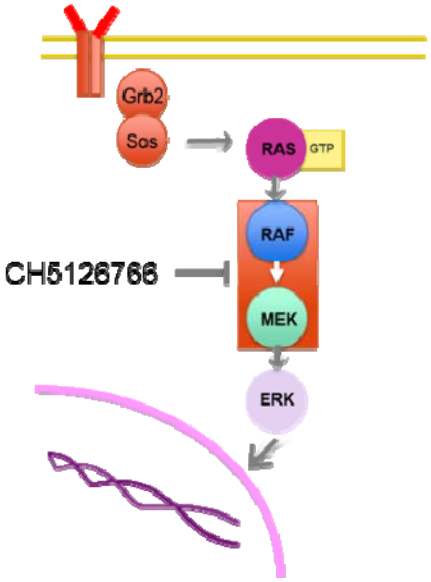
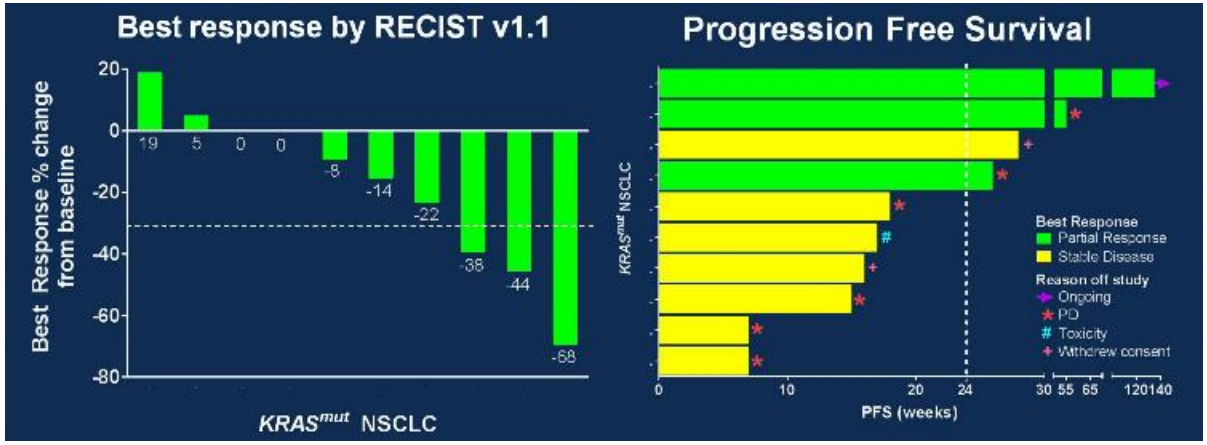
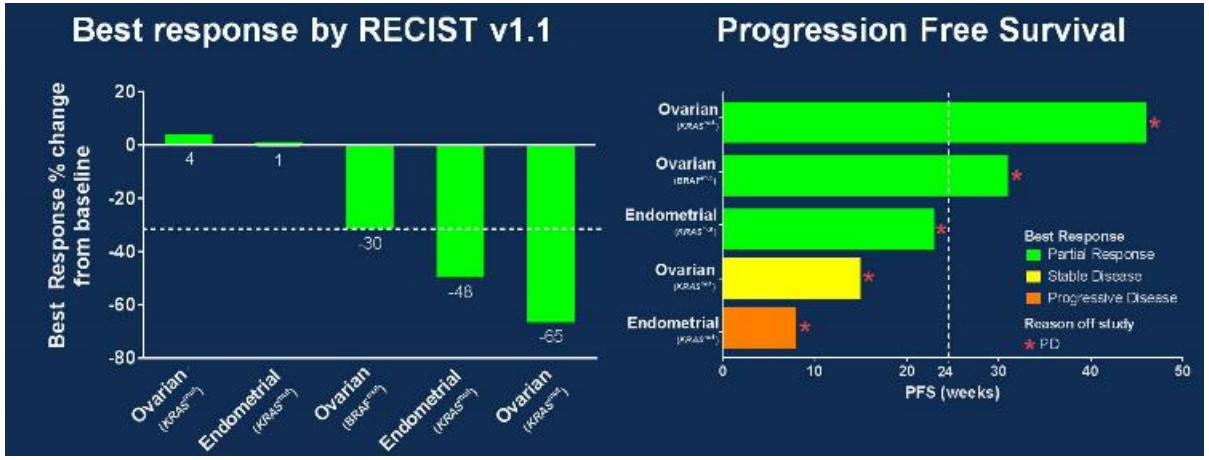
CKI27

Potent RAF/MEK Inhibitor in *KRAS*^{mut} NSCLC and *KRAS*^{mut}/*BRAF*^{mut} Gynaecological Cancers







Modified from Chenard-Poirier M. *et al,* ASCO 2017; CH5126766=CKI27

Targeting Treatment Options to Different Patients and Cancer Types

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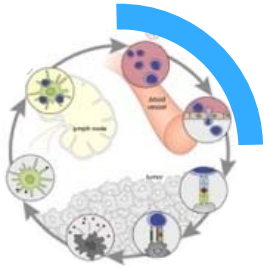
Melanoma Lung Bladder TNBC Colorectal Gastric Ovarian

IMMUNE INFLAMED

CD8+ T cells infiltrated, but non-functional

Accelerate or remove brakes on T-cell response

e.g. Tecentriq, Cotellic, navoximod (IDOi), aOX40, aTIGIT, aCEA/FAP IL-2v, aCSF-1R, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974)

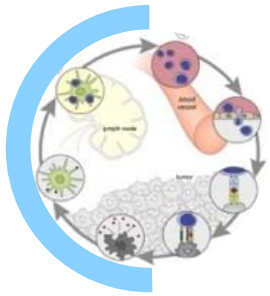


IMMUNE EXCLUDED

CD8+ T cells accumulated but have not efficiently infiltrated

Bring T-cells in contact with cancer cells

e.g. aVEGF, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974)



IMMUNE DESERT

CD8+ T cells absent from tumor and periphery

Increase number of antigen-specific T-cells or increase antigen presentation

e.g. aCD40, chemotherapy, radiotherapy, targeted therapies, TCBs (CEA TCB, CD20 TCB), TRAB (ERY974), PCV

TCB=T cell bispecific; TRAB=T-cell redirecting antibody; PCV=personalized cancer vaccine

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