中外製薬R&Dコール

中外製薬株式会社
ﾌﾟﾛｼﾞｪｸﾄ・ﾗｲﾌｻｲｸﾙ ﾏﾈｼﾞﾒﾝﾄﾕﾆｯﾄ
ｵﾝｺﾛｼﾞｰﾗｲﾌｻｲｸﾙﾏﾈｼﾞﾒﾝﾄ部長
宇津　恵

2017.6.29

すべての革新は患者さんのために

CHUGAI

Roche ロシュ グループ

将来見通し

本プレゼンテーションには、中外製薬の事業及び展望に関する将来見通しが含まれていますが、いずれも、既存の情報や様々な動向についての中外製薬による現時点での分析を反映しています。
実際の業績は、事業に及ぼすリスクや不確定な事柄により現在の見通しと異なることもあります。

本プレゼンテーションには、医薬品（開発品を含む）に関する情報が含まれていますが、それらは宣伝・広告や医学的なアドバイスを目的とするものではありません。

すべての革新は患者さんのために
CHUGAI
Roche ロシュ グループ

開発パイプライン
（2017年6月29日現在）

	Phase I	Phase II	Phase III	Filed
がん	CKI27（国内 / 海外） – 固形がん RG7596 / polatuzumab vedotin – 非ﾎｼﾞｷﾝﾘﾝﾊﾟ腫 RG7604 / taselisib – 固形がん RG7440 / ipatasertib – 固形がん GC33（RG7686）/ codrituzumab – 肝がん★ ERY974（海外） – 固形がん RG6078 – 固形がん		RG1273 / Perjeta – 乳がん（ｱｼﾞｭﾊﾞﾝﾄ） – 胃がん RG3502 / Kadcyla – 乳がん（ｱｼﾞｭﾊﾞﾝﾄ） GA101（RG7159）/ obinutuzumab – 低悪性度非ﾎｼﾞｷﾝﾘﾝﾊﾟ腫 RG435 / Avastin – 腎細胞がん RG7446 / atezolizumab – 非小細胞肺がん（ｱｼﾞｭﾊﾞﾝﾄ） – 小細胞肺がん – 尿路上皮がん – 筋層浸潤尿路上皮がん（ｱｼﾞｭﾊﾞﾝﾄ） – 腎細胞がん – 腎細胞がん(ｱｼﾞｭﾊﾞﾝﾄ) – 乳がん – 卵巣がん – 前立腺がん	RG7446 / atezolizumab – 非小細胞肺がん AF802（RG7853）/ Alecensa（海外） – 非小細胞肺がん(1L)

各相の臨床試験は、原則として投与の開始をもって試験開始としています

オレンジ：自社品
★：中外主導の国際共同治験

ASCO2017
Key Presentations Featuring Chugai Projects

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

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)]

ASCO2017
Key Presentations Featuring Chugai Projects

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

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

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

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

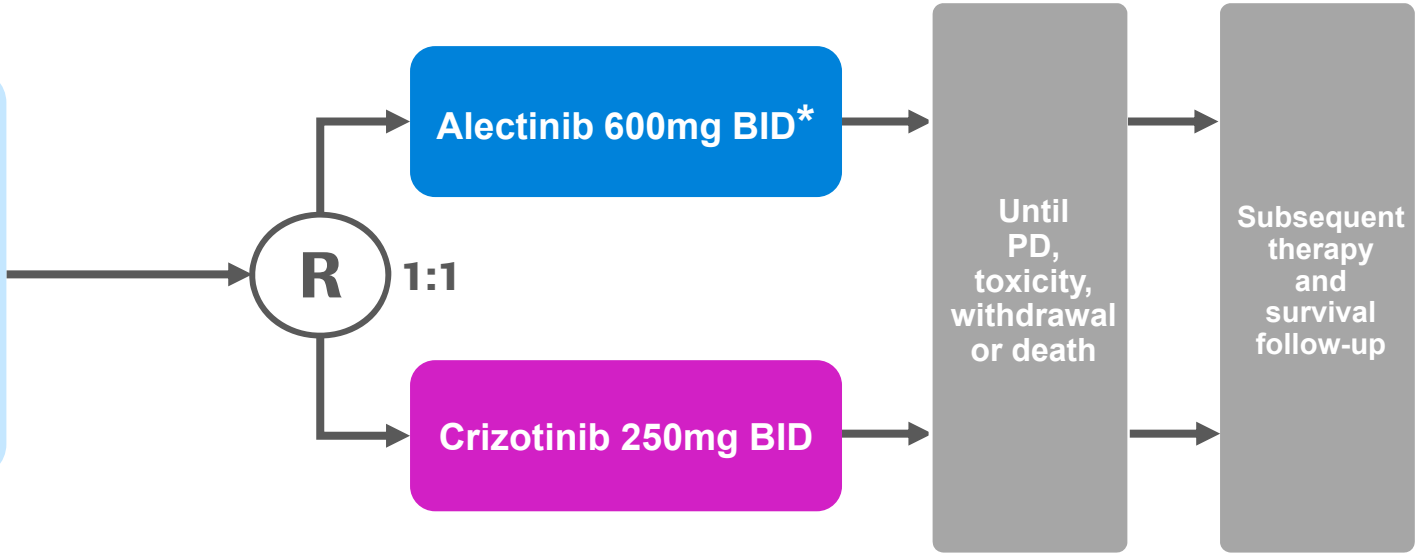
- Results from the biomarker-driven basket trial of RO5126766 (CH5126766), a potent RAF/MEK inhibitor, in RAS- or RAF- mutated malignancies including multiple myeloma [Abstract #2506 (oral)]

Alecensa
ALEX Study: Study Design

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

- 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

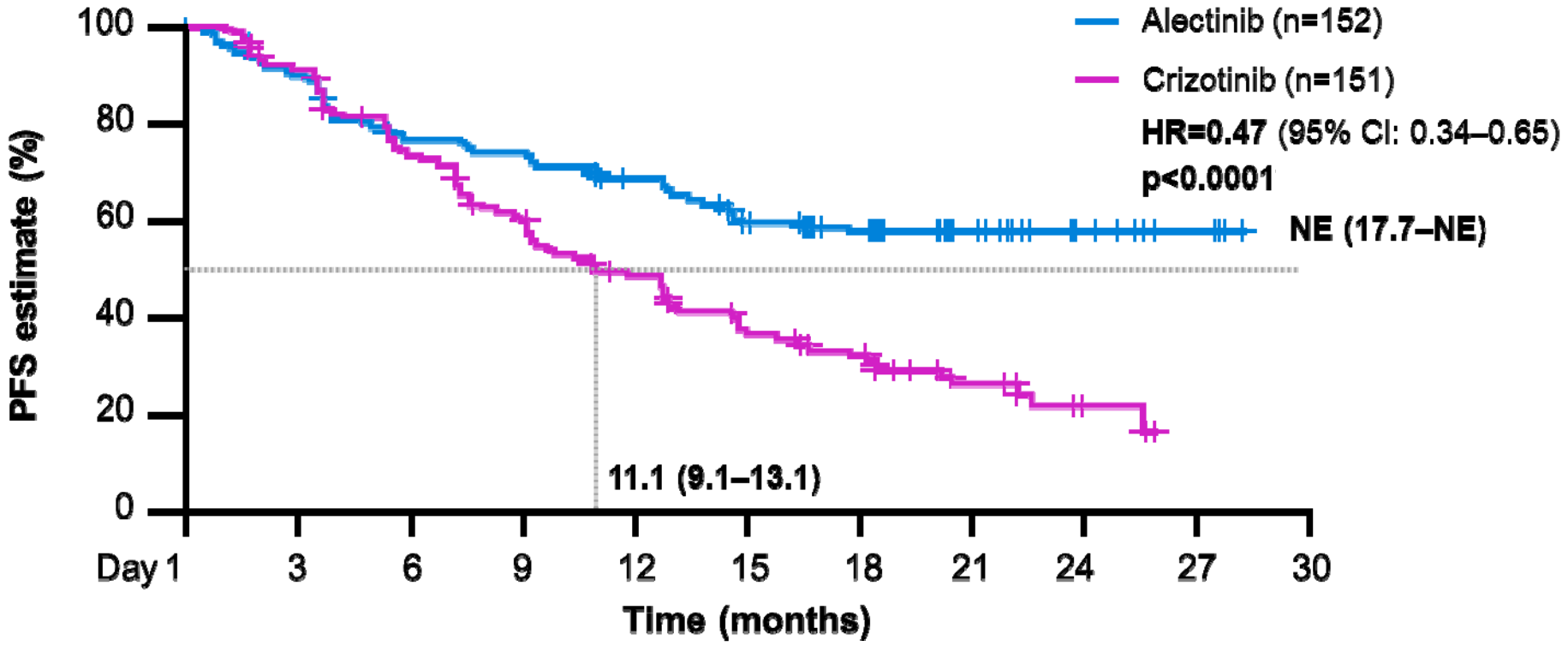
Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Alecensa
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

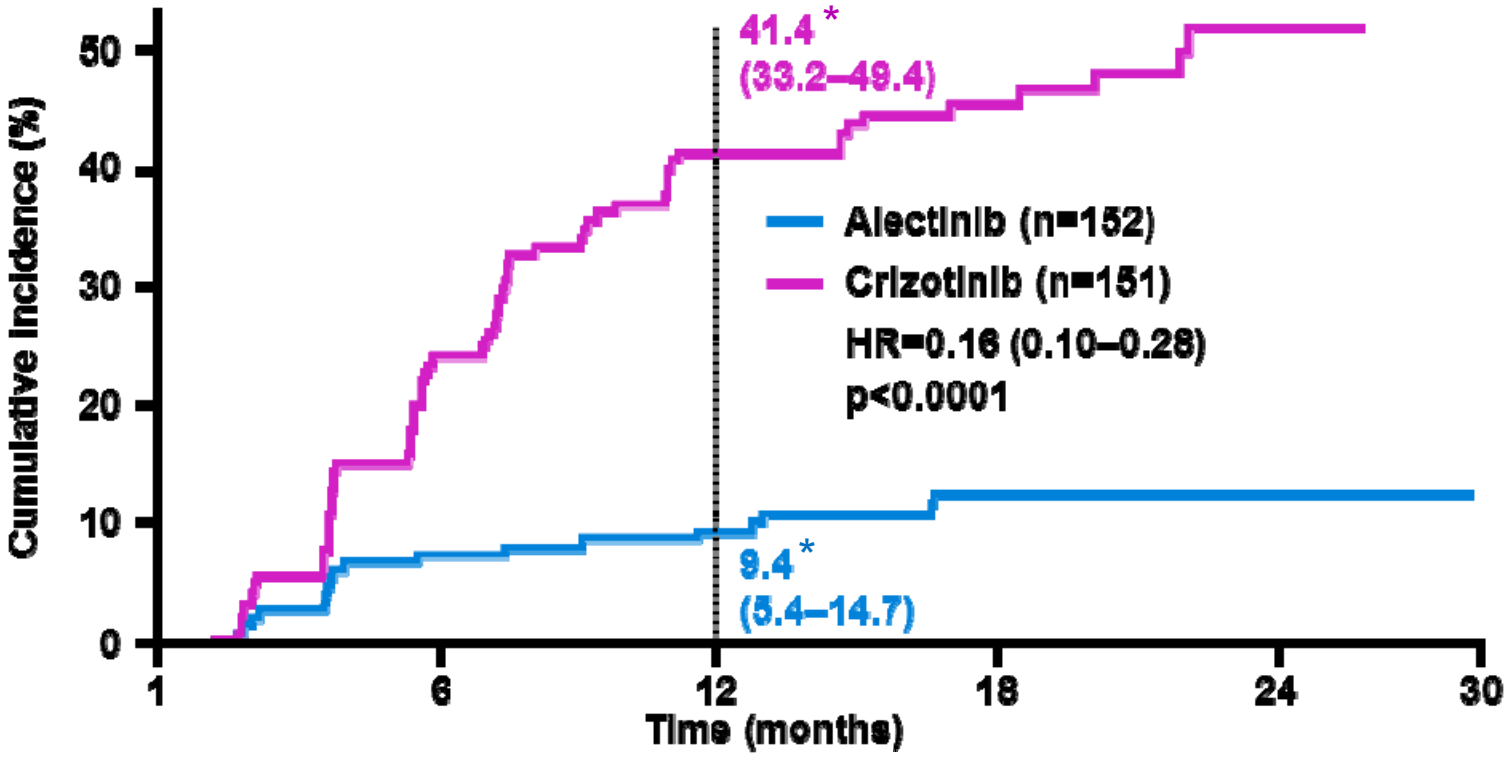
Alecensa
ALEX Study: Efficacy

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Alecensa
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

Innovation all for the patients

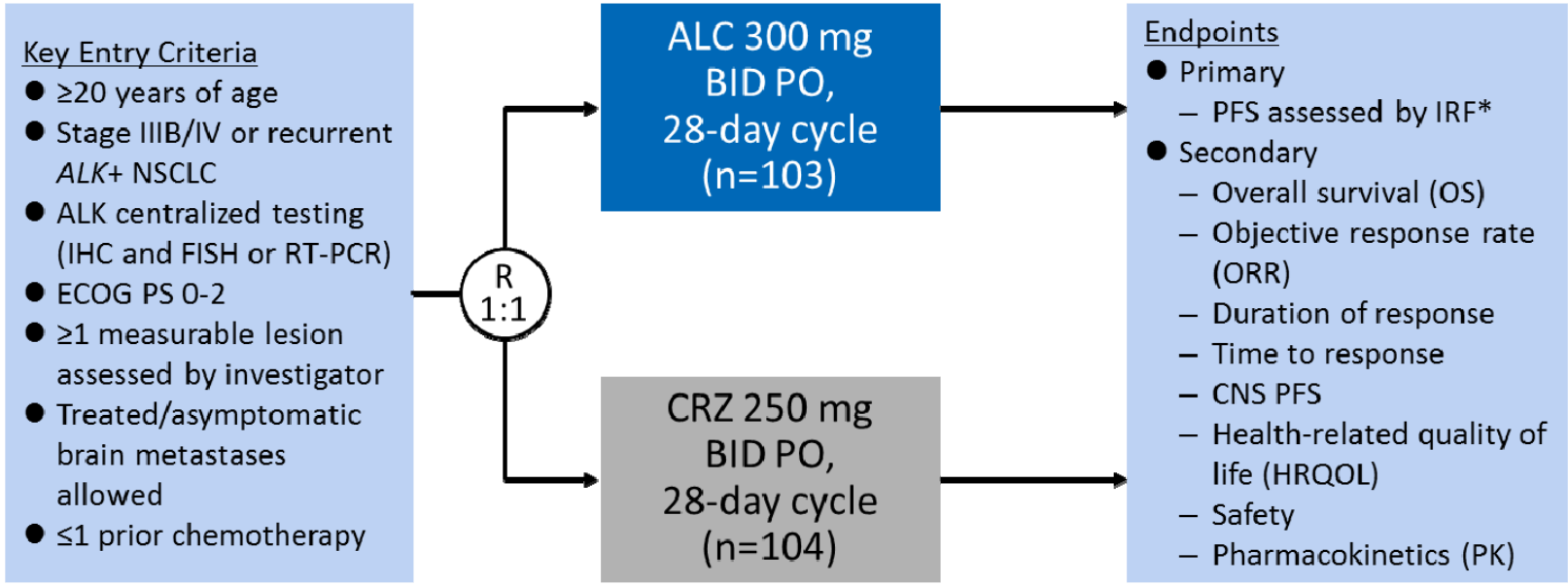
CHUGAI

Roche A member of the Roche group

Alecensa
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

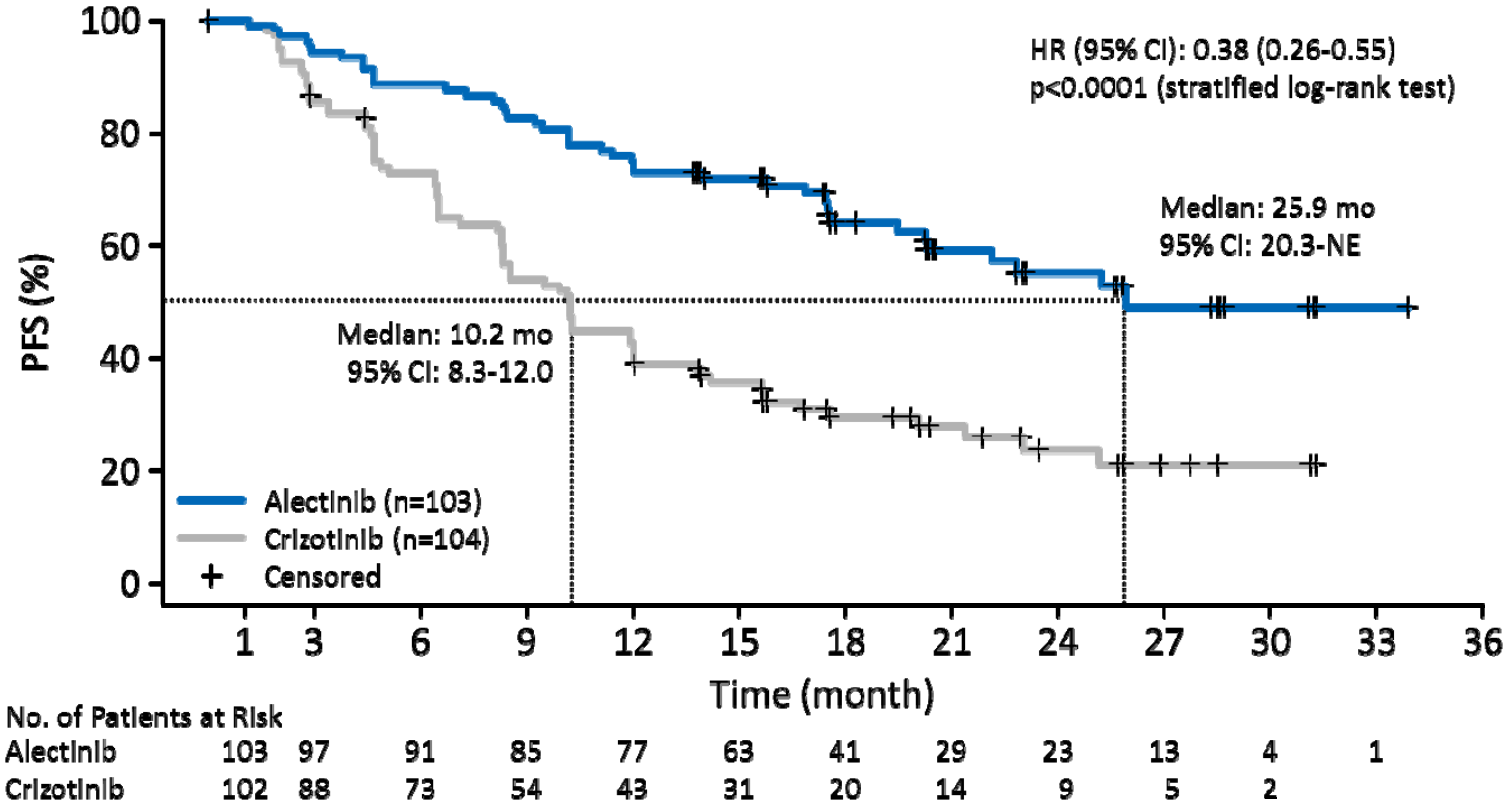
Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Alecensa
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

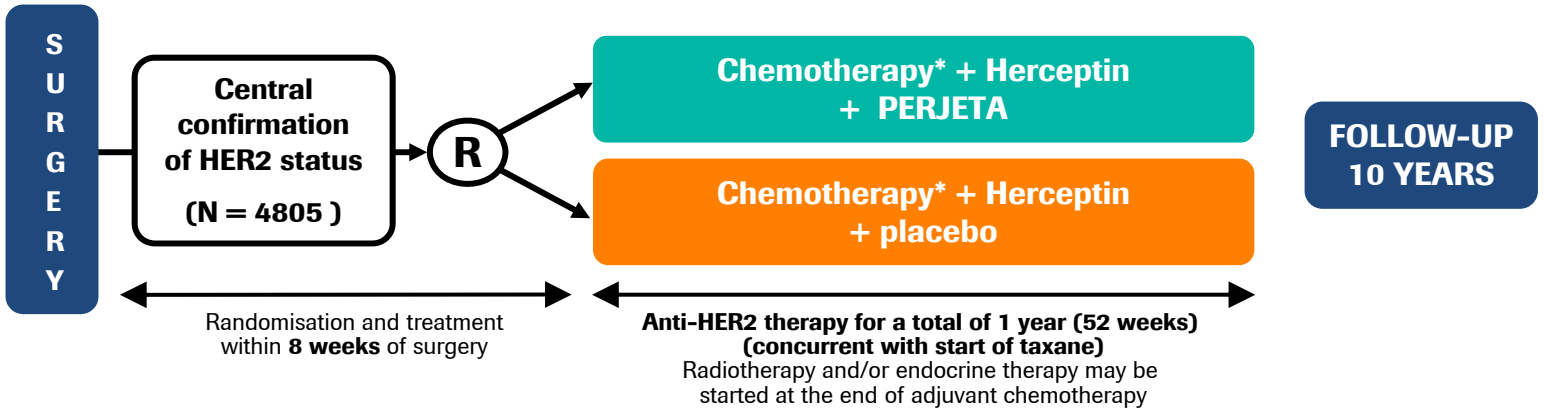
Pertuzumab
APHINITY: Study Design

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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

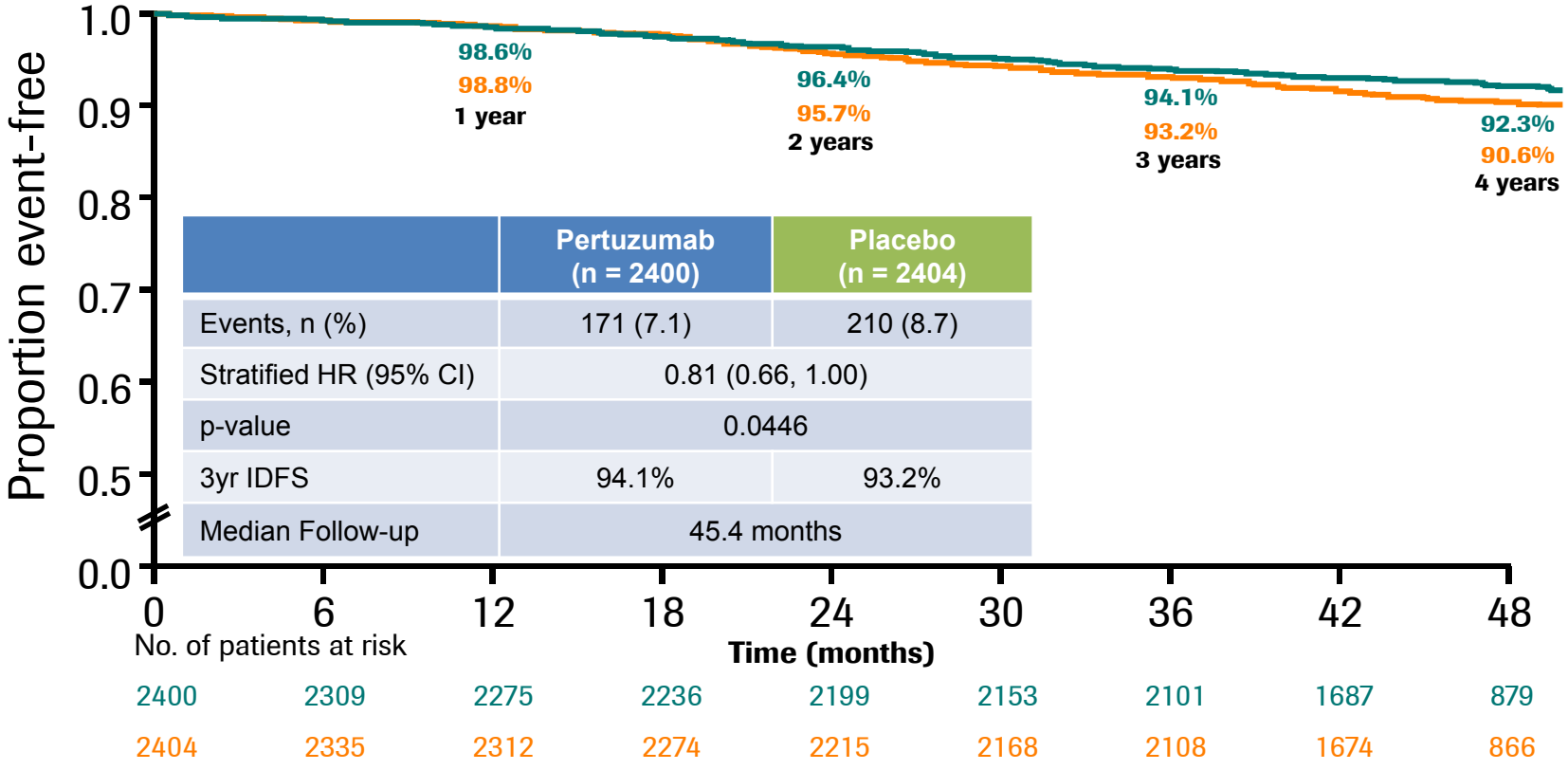
Modified from Minckwitz G. *et al,* ASCO 2017

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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	

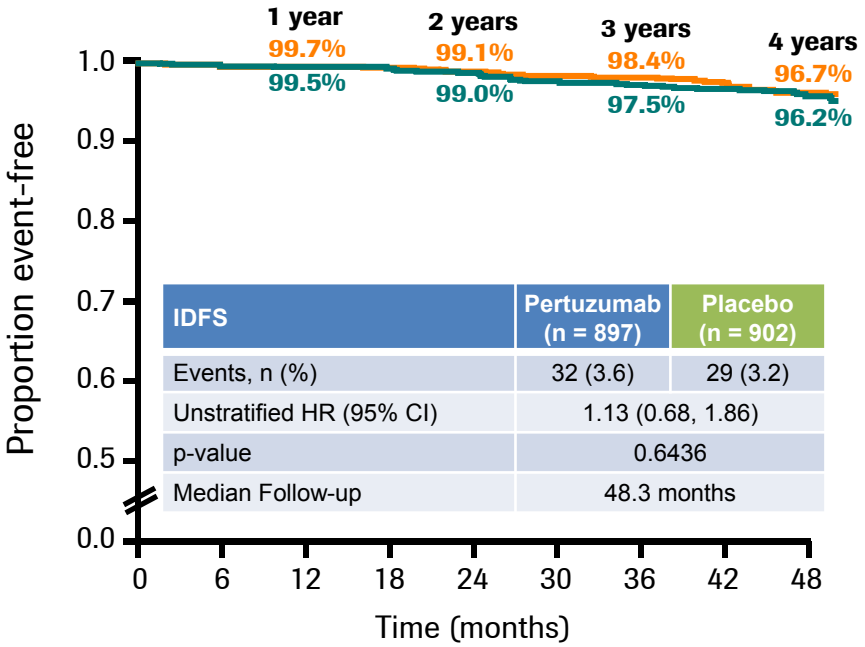
- The safety profiles were consistent with those seen in previous studies.

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

Pertuzumab
APHINITY: Subgroup Analysis (Nodal Status)

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

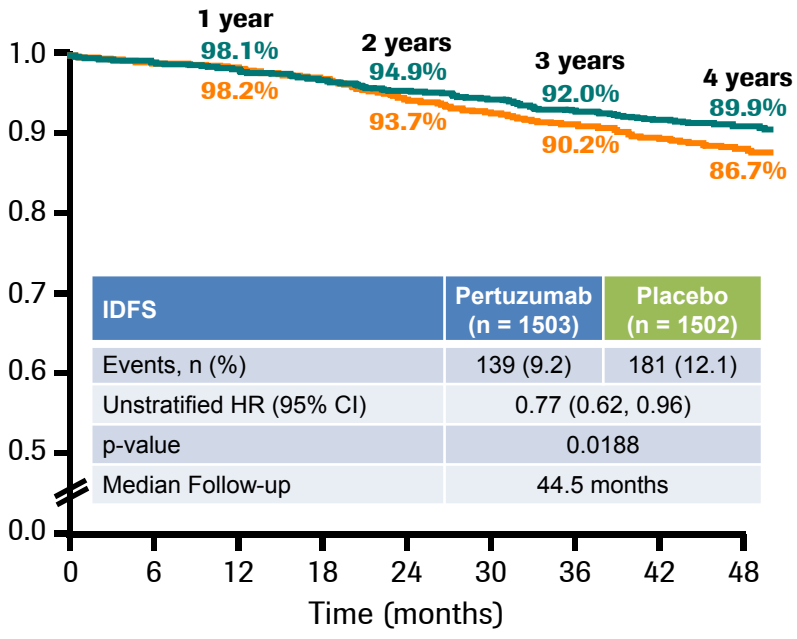
Lymph node-negative subgroup (n = 1799)



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	

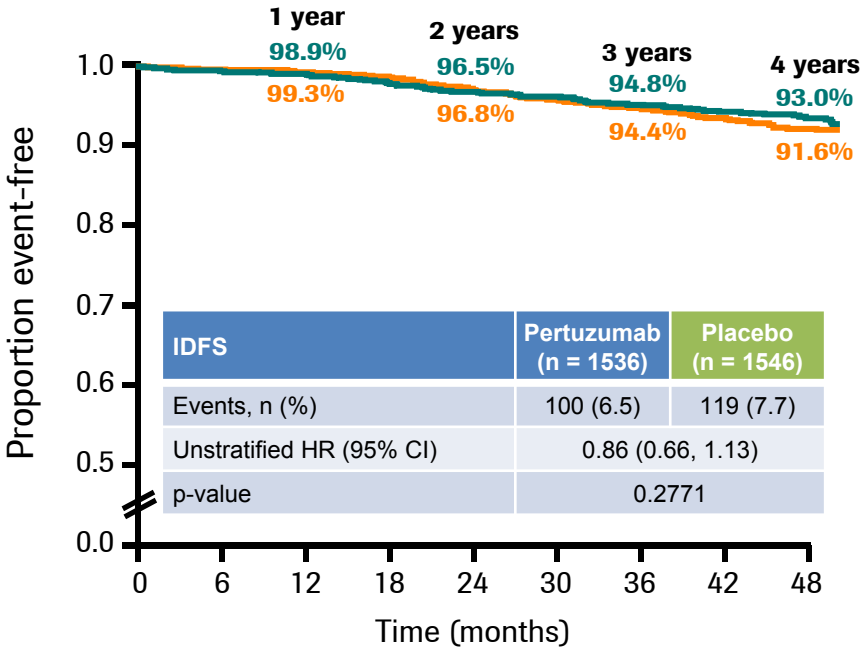
No. of patients at risk									
	1503	1444	1419	1387	1358	1327	1283	912	423
	1502	1453	1439	1408	1359	1319	1264	882	405

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

Pertuzumab
APHINITY: Subgroup Analysis (HR Status)

Innovation all for the patients
CHUGAI
Roche A member of the Roche group

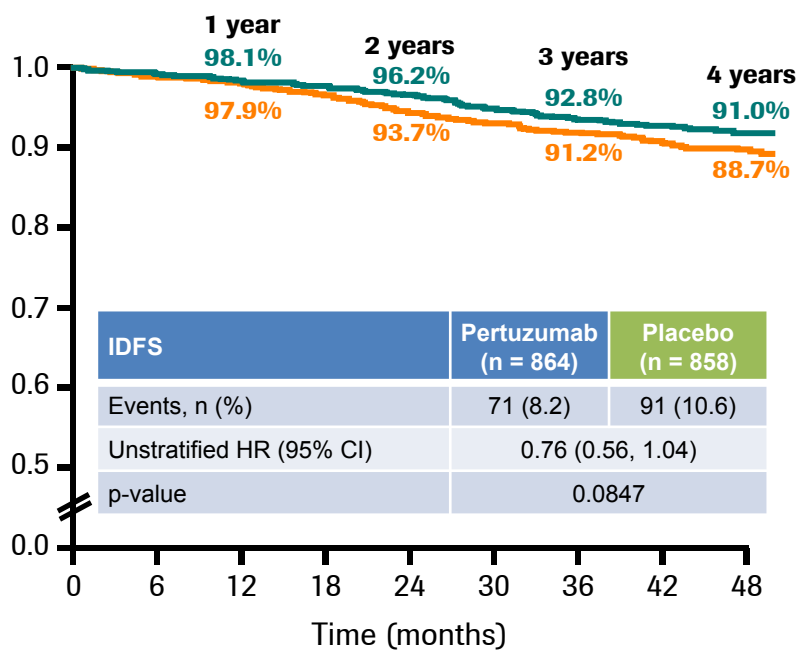
HR-positive subgroup (n = 3082)



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

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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)

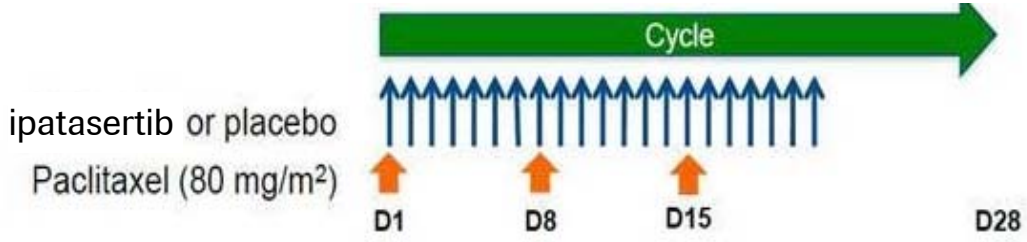
R 1:1

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

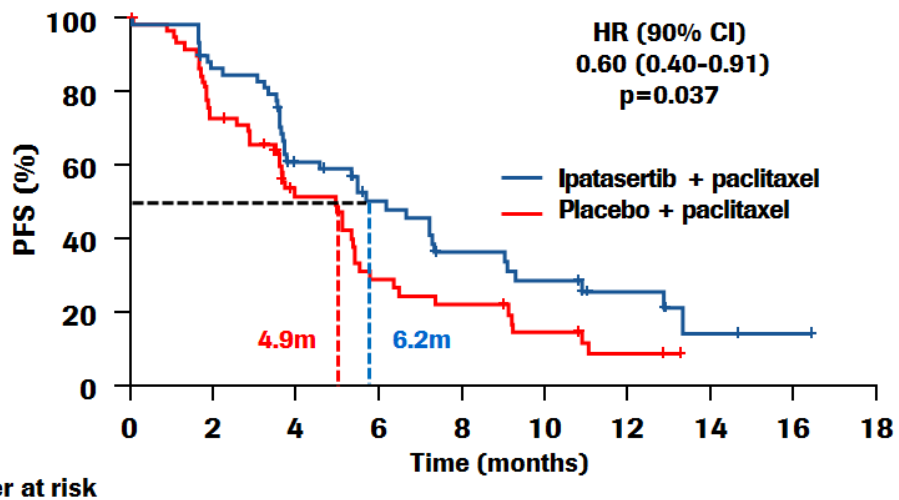
Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Ipatasertib
LOTUS: Efficacy (PFS)

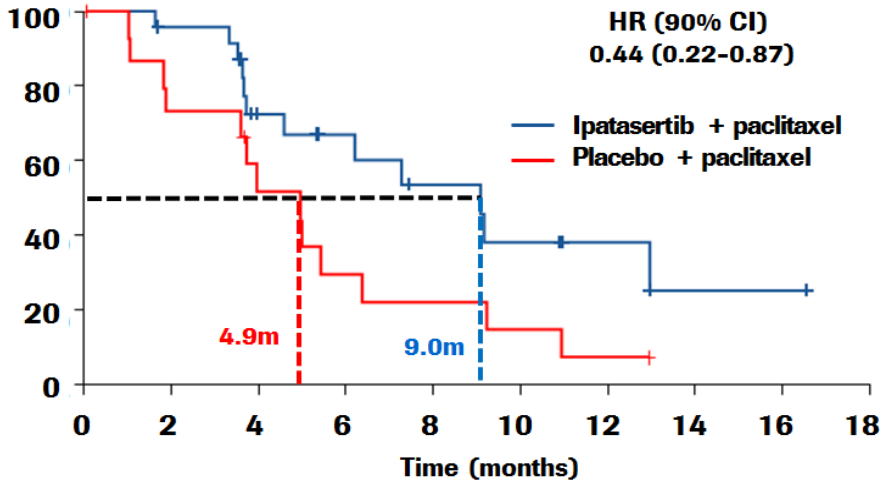
ITT population



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		

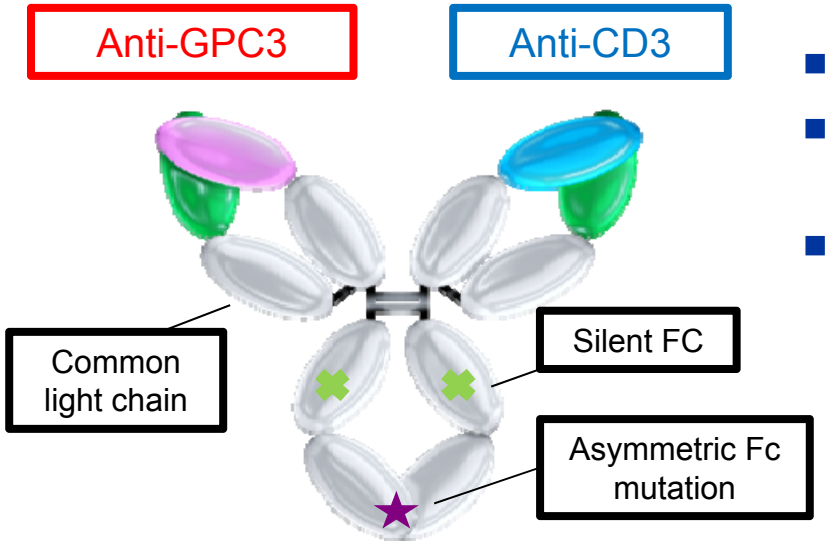
Modified from Dent R. *et al,* ASCO 2017

ERY974 (TRAB)

Innovation all for the patients

CHUGAI

Roche A member of the Roche group



- 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

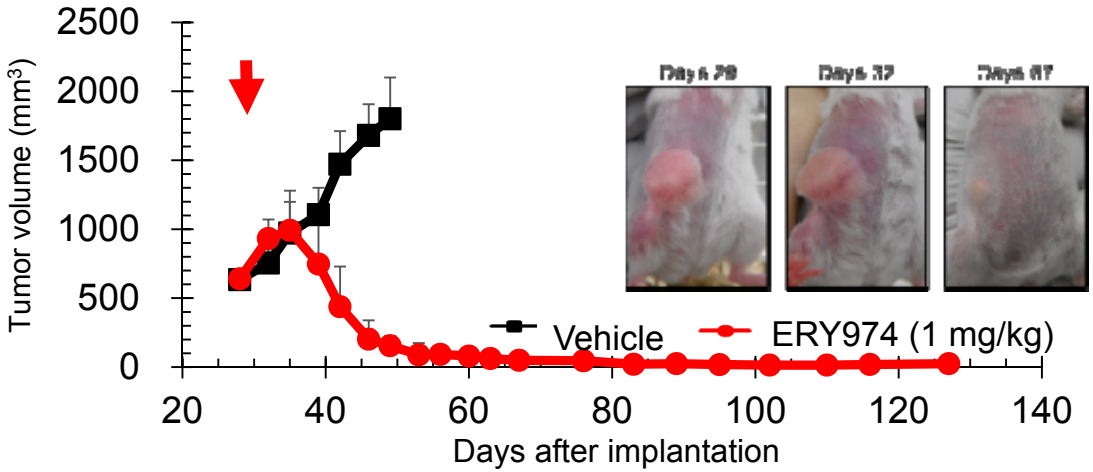
Modified from Hashimoto K. *et al,* ASCO 2017; TRAB=T-cell redirecting antibody

Efficacy of ERY974 in Preclinical Models

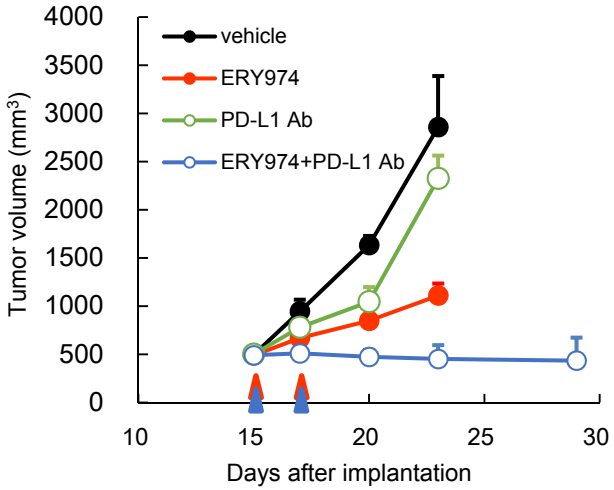
Innovation all for the patients
CHUGAI
Roche A member of the Roche group

(Sano Y. et al., AACR2017)

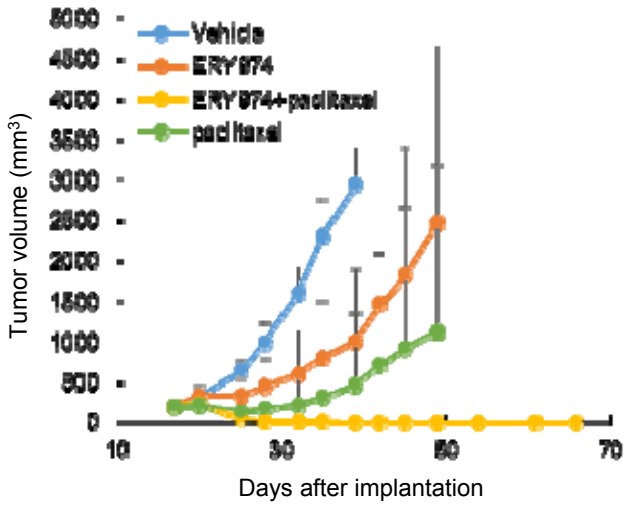
ERY974 monotherapy (KYSE70)



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



ERY974 + paclitaxel (NCI-H446)



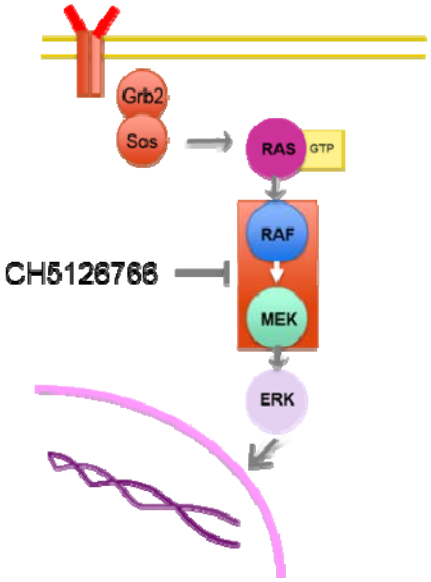
Innovation all for the patients

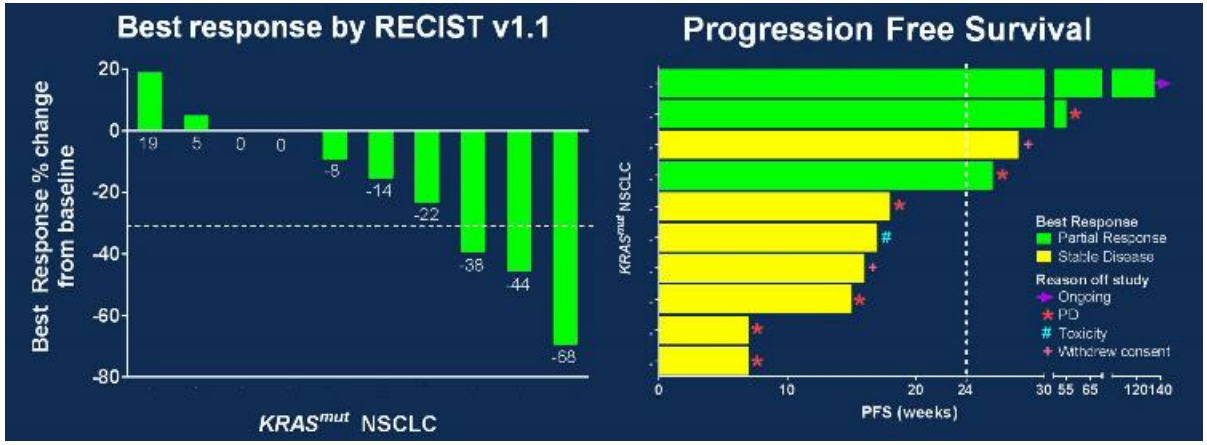
CHUGAI

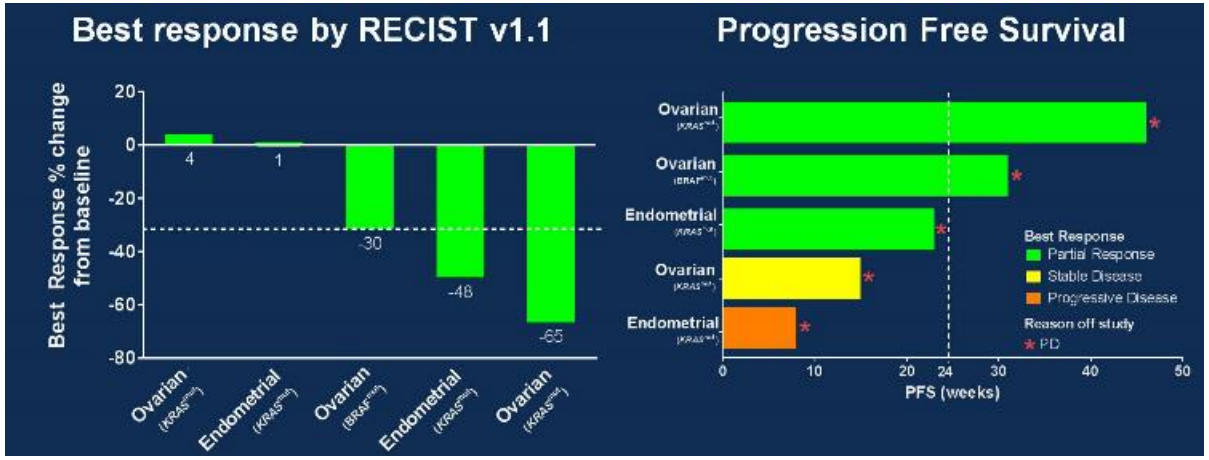
Roche A member of the Roche group

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

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

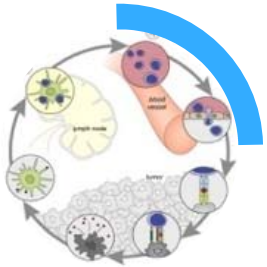
Melanoma Lung Bladder TNBC Colorectal Gastric Ovarian

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)

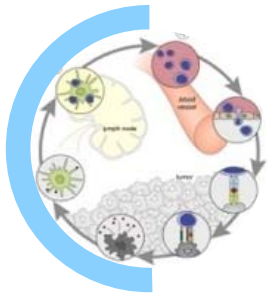


IMMUNE EXCLUDED

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

お問い合わせ先：広報IR部

投資家の皆様：
インベスターリレーションズグループ

Tel : 03-3273-0554
e-mail : ir@chugai-pharm.co.jp
担当：笹井、櫻井、清水、島村