유한양행 기업설명회

2025. 1Q

유한양행

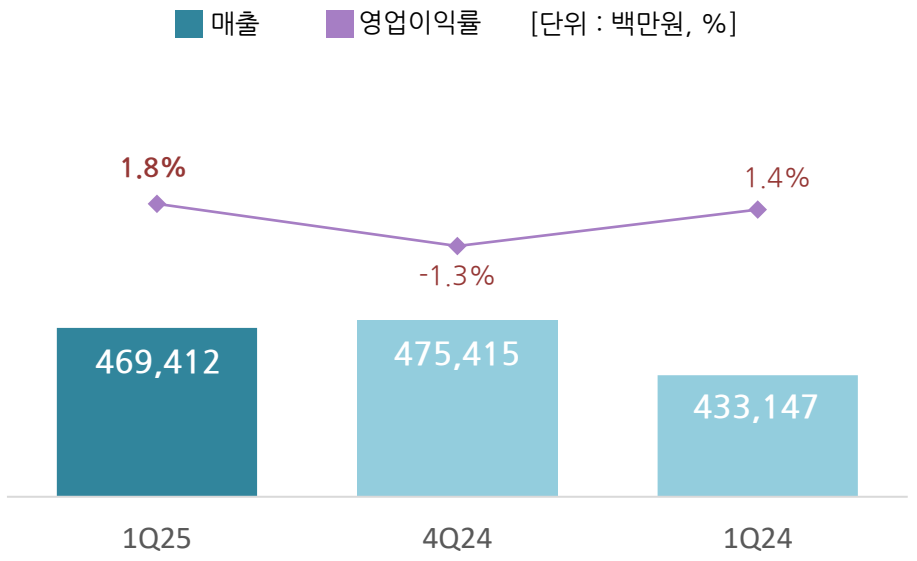
2025년 1분기 실적 분석

유한양행

별도

[단위 : 백만원]

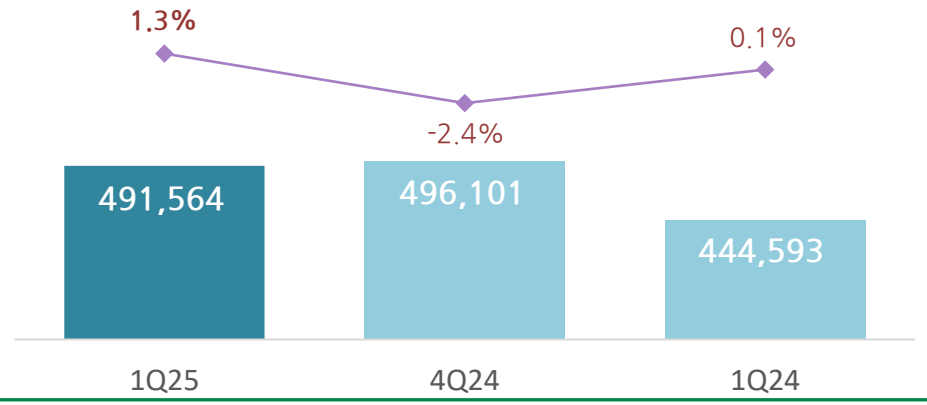
과 목	1Q25	4Q24	QoQ	1Q24	YoY
매출액	469,412	475,415	-1.3%	433,147	8.4%
라이선스 수익	3,976	3,963	0.3%	2,549	56.0%
매출원가	336,415	337,991	-0.5%	308,591	9.0%
매출원가율	71.7%	71.1%	0.6%p	71.2%	0.5%p
R&D 비용	50,199	64,734	-22.5%	45,683	9.9%
광고선전비	12,478	14,900	-16.3%	21,685	-42.5%
영업이익	8,645	-6,233	흑자 전환	6,142	40.8%
당기순이익	39,331	12,089	225.3%	36,369	8.1%



연결

[단위 : 백만원]

과 목	1Q25	4Q24	QoQ	1Q24	YoY
매출액	491,564	496,101	-0.9%	444,593	10.6%
영업이익	6,420	-11,817	흑자 전환	577	1012.3%
당기순이익	10,009	-23,102	흑자 전환	10,812	-7.4%



2025년 1분기 사업부 및 주요 품목 실적

유한양행

분기별 사업부 실적 (별도기준)

[단위 : 백만원]

구분		1Q25	4Q24	QoQ	1Q24	YoY
약품 사업	비처방	54,313	53,746	1.1%	46,907	15.8%
	처방	275,468	297,620	-7.4%	262,621	4.9%
	소계	329,781	351,366	-6.1%	309,528	6.5%
생활건강사업		46,741	53,517	-12.7%	44,454	5.1%
해외사업		87,363	65,130	34.1%	74,107	17.9%
라이선스 수익		3,976	3,963	0.3%	2,549	56.0%
기타(임대, 수탁 등)		1,551	1,439	7.8%	2,509	-38.2%
매출액		469,412	475,415	-1.3%	433,147	8.4%

주요 품목 실적

[단위 : 백만원]

구분	품목	1Q25	YoY	1Q24
비처방	안티푸라민(소염진통)	8,204	-12.9%	9,417
	엘레나(유산균)	5,826	-12.5%	6,658
	마그비(영양제)	5,089	25.2%	4,066
	비타민씨(영양제)	4,751	39.5%	3,407
	비판텐(상처치료제)	3,708		
처방	자디앙(당뇨병)	25,301	13.6%	22,262
	트윈스타(고혈압)	21,271	-2.1%	21,717
	트라젠타(당뇨병)	20,247	-20.0%	25,309
	비리어드(B형간염)	17,904	0.1%	17,879
	빅타비(HIV)	16,749	0.3%	16,697
	로수바미브(이상지질혈증)	16,666	2.1%	16,322
	베믈리디(B형간염)	15,884	20.3%	13,203
	글리벡(백혈병)	12,560	1.9%	12,323
	코푸시럽/정(호흡기)	12,350	-17.2%	14,914
	페마라(항암제)	7,001	36.8%	5,117

R&D 현황

주요 혁신신약 파이프라인

유한양행

* Black 합성신약, Blue 바이오신약

약물	타겟	적응증	후보물질	비임상	임상 1상	임상 2상	임상 3상	Licensor	Licensee
LAZERTINIB	EGFR 돌연변이 3세대 TKI	EGFR돌연변이 비소세포폐암	단독요법 (유한) 글로벌 3상 Amivantamab 병용요법 (J&J) 글로벌 3상					GENOSCO	Johnson&Johnson Innovative Medicine
YH14618 (Remedisc)	TGF-β	퇴행성 디스크						EnsolBio sciences	SpineBiopharma
YH12852 (PCS12852)	5-HT receptor	위마비증							Processa Pharmaceuticals
YH35324	IgE	Allergy (CSU, 천식, AD)						GI innovation	
YH32367	Her2/4-1BB	유방암, 위암, 담관암 등						ablbio	
YH42946	Her2, EGFR	Her2돌연변이 폐암, 위암 등						JINTS BIO	
YH35995	GCS	고셔병, 파브리병						GC	
YH32364	EGFR/4-1BB	두경부암, 위암, 대장암 등						ablbio	
YH45057	Androgen receptor	전립선암						Ubix Therapeutics	
YH44529	SOS1	고형암						Cyrus KANAPH	

Progress & Integrity

AACR ANNUAL MEETING 2025

April 25 - 30, 2025
McCormick Place Convention Center
Chicago, IL

YH32364 (ABL104), a bispecific antibody against EGFR and 4-1BB, demonstrates potent anti-tumor efficacy through tumor-directed 4-1BB agonism

Jae-Won Lee[1], Yangsoon Lee[2], Eunjung Lee[1], Hanna Hong[1], Byeong-Yun Ahn[1], Jangbeen Kyung[1], Young Bong Park[1], Junhwan Kim[1], Kyeongsu Park[2], Wonjun Son[2], Jaehyun Eom[2], Hanbyul Lee[2], Kyeongnang Moon[2], Yelim Park[2], Jonghwa Won[2], Se-Woong Oh[1], Yeul Hong Kim[1]

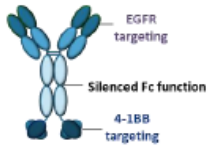
[1]Yuhan Corporation, Seoul, Republic of Korea, [2]ABL Bio Inc., Gyeonggi-do, Republic of Korea

2025 AACR Abstract Presentation Number: 6084

Background

YH32364 (ABL104), Anti-EGFR/4-1BB bispecific antibody

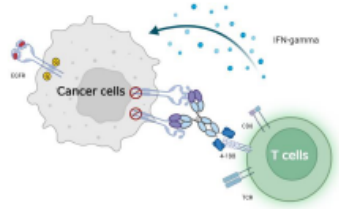
Structure



- Tumor-directed EGFR/4-1BB bispecific antibody engineered to amplify tumor-localized super-agonist activity of 4-1BB while minimizing the risk of peripheral toxicity
- IgG1 isotype antibody with silenced Fc effector function

Mechanism of action

- Induction of T cell activation and survival through EGFR expressing tumor-specific 4-1BB stimulation
- Growth signal blocking via EGFR receptor binding in tumor



Indications

- EGFR positive solid cancers: HNSCC, lung cancer, colon cancer *etc.*

Competitive advantage

- Compared to EGFR-mAb or TKI, YH32364 is expected to have
  - Long-term clinical efficacy due to tumor-specific immune-memory
  - Anti-tumor effect via EGFR signaling inhibition in patients with EGFR alteration
  - Minimal liver toxicity risk through Fc-engineering

Development stage

- IND submitted in Jan 2025 (Korea MFDS)

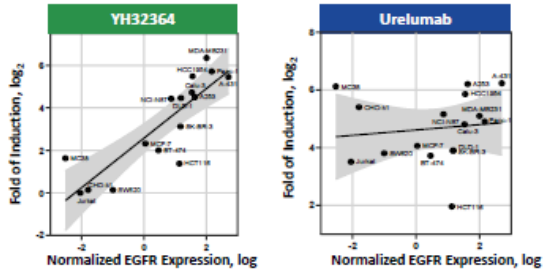
Results

YH32364 exhibits potent binding affinities to the targets

Table. 1. The binding affinities to targets

	Assay system		YH32364	Benchmark anti-4-1BB mAb	Cetuximab
Binding affinity	SPR K_D (nM)	h4-1BB	3.7	1.8	NA
		hEGFR	0.76	NA	0.87
In vitro Potency	4-1BB bioassay of DLD-1 (EC_{50}, nM)		0.031	0.294	NA

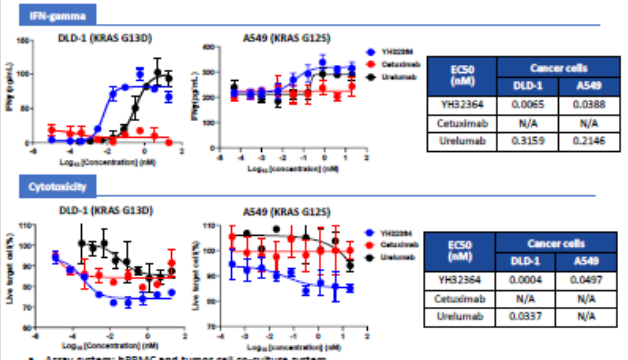
YH32364 induces to 4-1BB activation through EGFR expression level-dependent binding



- Assay system: 4-1BB bioassay / EGFR expression was normalized relative to MDA-MB-231
- Urelumab: in house preparation

Fig. 1. EGFR-dependent 4-1BB activation

YH32364 induces T cell activation and target cell lysis in a dose-dependent manner against EGFR-expressing cancer cells with a KRAS mutation



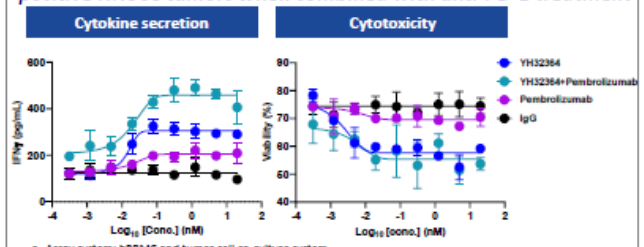
EC50 (nM)	Cancer cells	
	DLD-1	A549
YH32364	0.0065	0.0388
Cetuximab	N/A	N/A
Urelumab	0.3159	0.2146

EC50 (nM)	Cancer cells	
	DLD-1	A549
YH32364	0.0004	0.0497
Cetuximab	N/A	N/A
Urelumab	0.0337	N/A

- Assay system: hPBMC and tumor cell co-culture system
- Urelumab: in house preparation

Fig. 2. *In vitro* hPBMC based cytokine secretion and target cell lysis

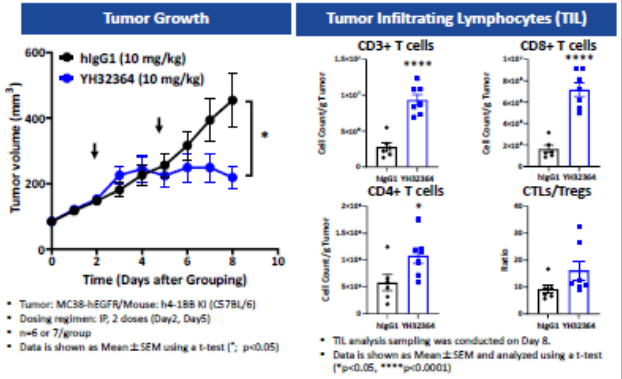
YH32364 shows strong in vitro anti-tumor efficacy against EGFR-positive HNSCC tumors when combined with anti-PD-1 treatment



- Assay system: hPBMC and tumor cell co-culture system

Fig. 3. *In vitro* efficacy of YH32364 plus pembrolizumab in CAL-27 cells

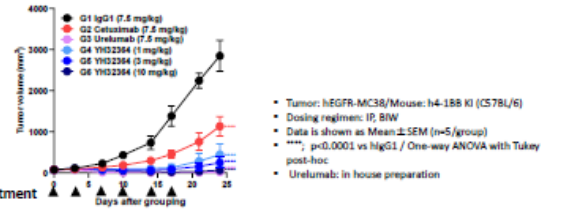
YH32364 treatment enhances immune cell infiltration into the tumors



- Tumor: MC38-hEGFR/Mouse: h4-1BB KI (C57BL/6)
- Dosing regimen: IP, 2 doses (Day2, Day5)
- n=6 or 7/group
- Data is shown as Mean±SEM using a t-test (*; p<0.05)
- TIL analysis sampling was conducted on Day 8.
- Data is shown as Mean±SEM and analyzed using a t-test (*p<0.05, ****p<0.0001)

Fig. 4. Immune cell profiling in tumor from h4-1BB KI mouse

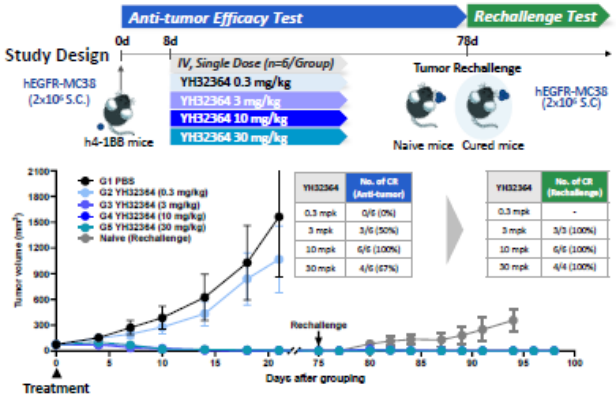
YH32364 shows a potent anti-tumor effect in 4-1BB KI mice



- Tumor: hEGFR-MC38/Mouse: h4-1BB KI (C57BL/6)
- Dosing regimen: IP, BIW
- Data is shown as Mean±SEM (n=5/group)
- ****; p<0.0001 vs hIgG1 / One-way ANOVA with Tukey post-hoc
- Urelumab: in house preparation

Fig. 5. *In vivo* efficacy in hEGFR-MC38 bearing 4-1BB KI mice

Single treatment of YH32364 shows prolonged anti-tumor efficacy against EGFR-expressing tumor via immune memory

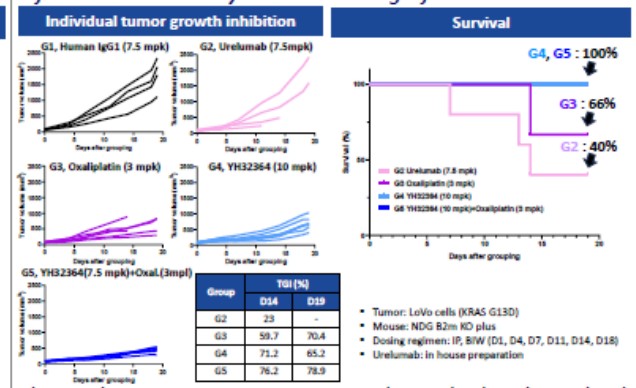


YH32364	No. of CR (Anti-tumor)
0.3 mpk	0/6 (0%)
3 mpk	3/6 (50%)
10 mpk	6/6 (100%)
30 mpk	4/6 (67%)

YH32364	No. of CR (Rechallenge)
0.3 mpk	-
3 mpk	3/3 (100%)
10 mpk	6/6 (100%)
30 mpk	4/4 (100%)

Fig. 6. Immune memory by YH32364 treatment confers durable TGI

YH32364 demonstrates robust anticancer efficacy and favorable tolerability in hPBMC xenograft mouse models



Group	TGI (%)	
	D14	D19
G2	23	-
G3	59.7	70.4
G4	71.2	65.2
G5	76.2	78.9

- Tumor: LoVo cells (KRAS G13D)
- Mouse: NDG B2m KO plus
- Dosing regimen: IP, BIW (D1, D4, D7, D11, D14, D18)
- Urelumab: in house preparation

Fig. 7. anti-tumor effect and favorable safety in combination with oxaliplatin

YH32364 is well tolerated in 4-week repeat dose cynomolgus monkeys GLP toxicology study

Table. 2. The study design for 4-week repeated tox study

Group		Dose level (mg/kg)	Dosing	No. of animals	
				Male	Female
G1	Vehicle	0	QW, IV, 4 doses total	5*	5*
G2	YH32364	10		3	3
G3	YH32364	30		3	3
G4	YH32364	100		5*	5*

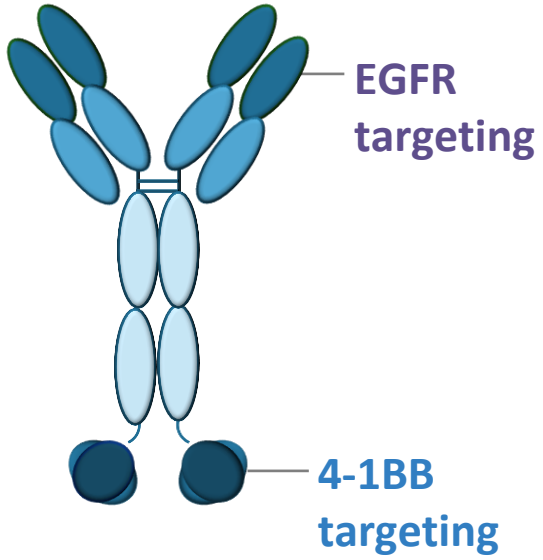
*: includes two additional animals for recovery phase

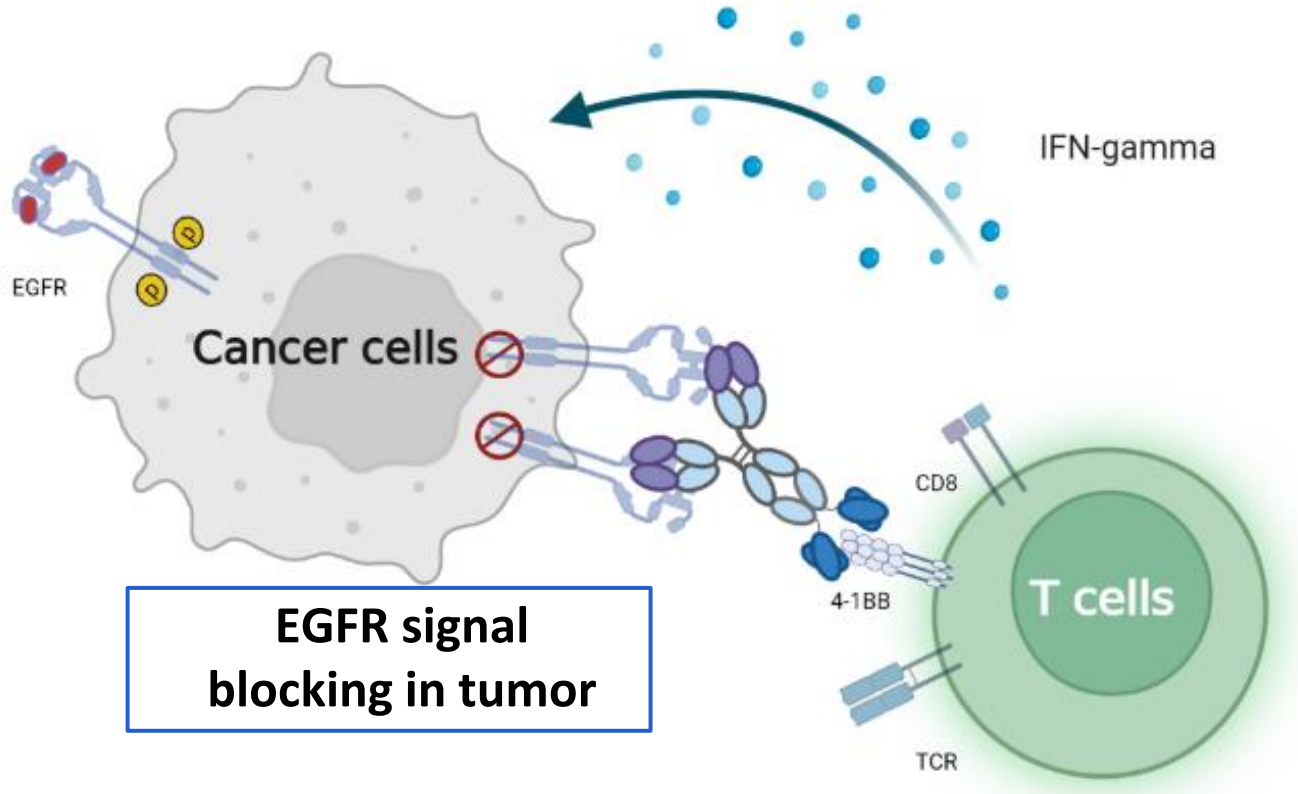
- Mortality/Body weight : No mortality and no YH32364-related body weight changes in all animals
- Clinical chemistry : No YH32364-related changes in hematology, clinical chemistry, and urinalysis effects (No increases in ALT and AST)
- Safety Pharmacology : No YH32364-related changes in abnormal ECG waveforms or arrhythmias, CNS, Respiratory evaluation
- Immunotoxicity : No YH32364-related effects in immunotyping (helper T cells, cytotoxic T cells, B cells, or NK cells), cytokine analysis (IFN-γ, IL-2, IL-4, IL-6, IFN-γ or TNF-α)
- NOAEL: 30 mg/kg, HNSTD: 100 mg/kg

Conclusions

- YH32364 exhibited remarkable *in vitro* and *in vivo* effects via anti-tumor immunity
- YH32364 has been shown to be effective when utilized in combination with anti-PD1 and/or chemo-therapy
- YH32364 could be a promising therapeutic drug for cancer patients with EGFR expression, with favorable tolerability

YH32364: EGFR/4-1BB bispecific antibody

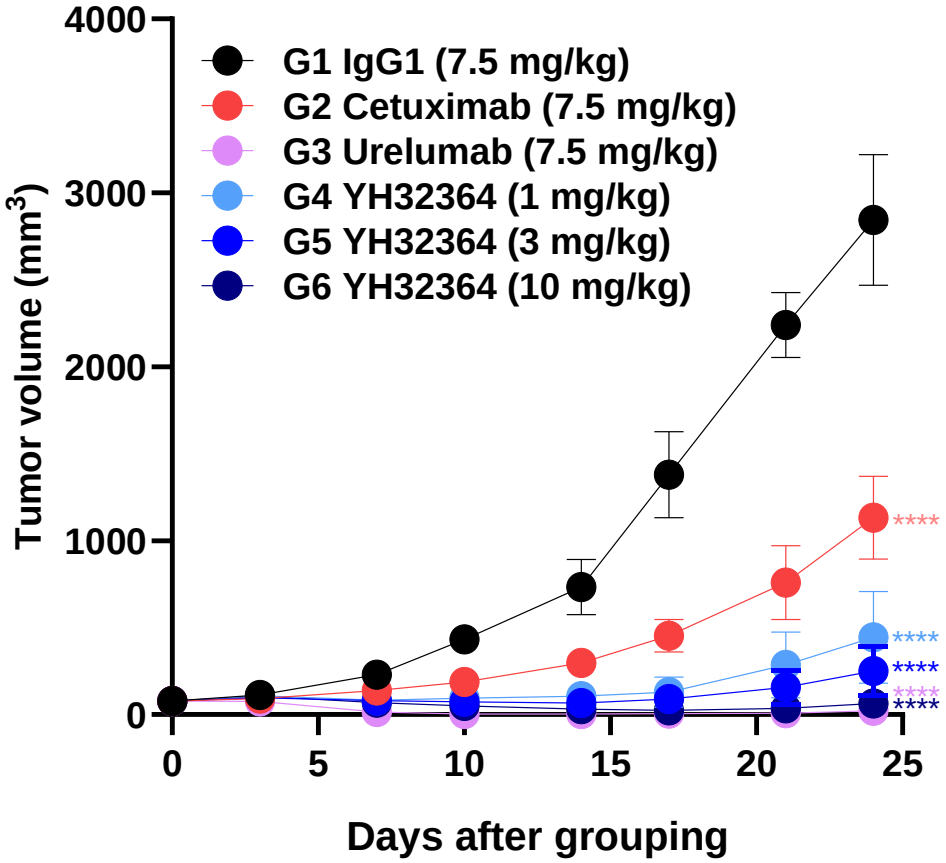




EGFR signal blocking in tumor

Co-stimulation effect for T cell activation

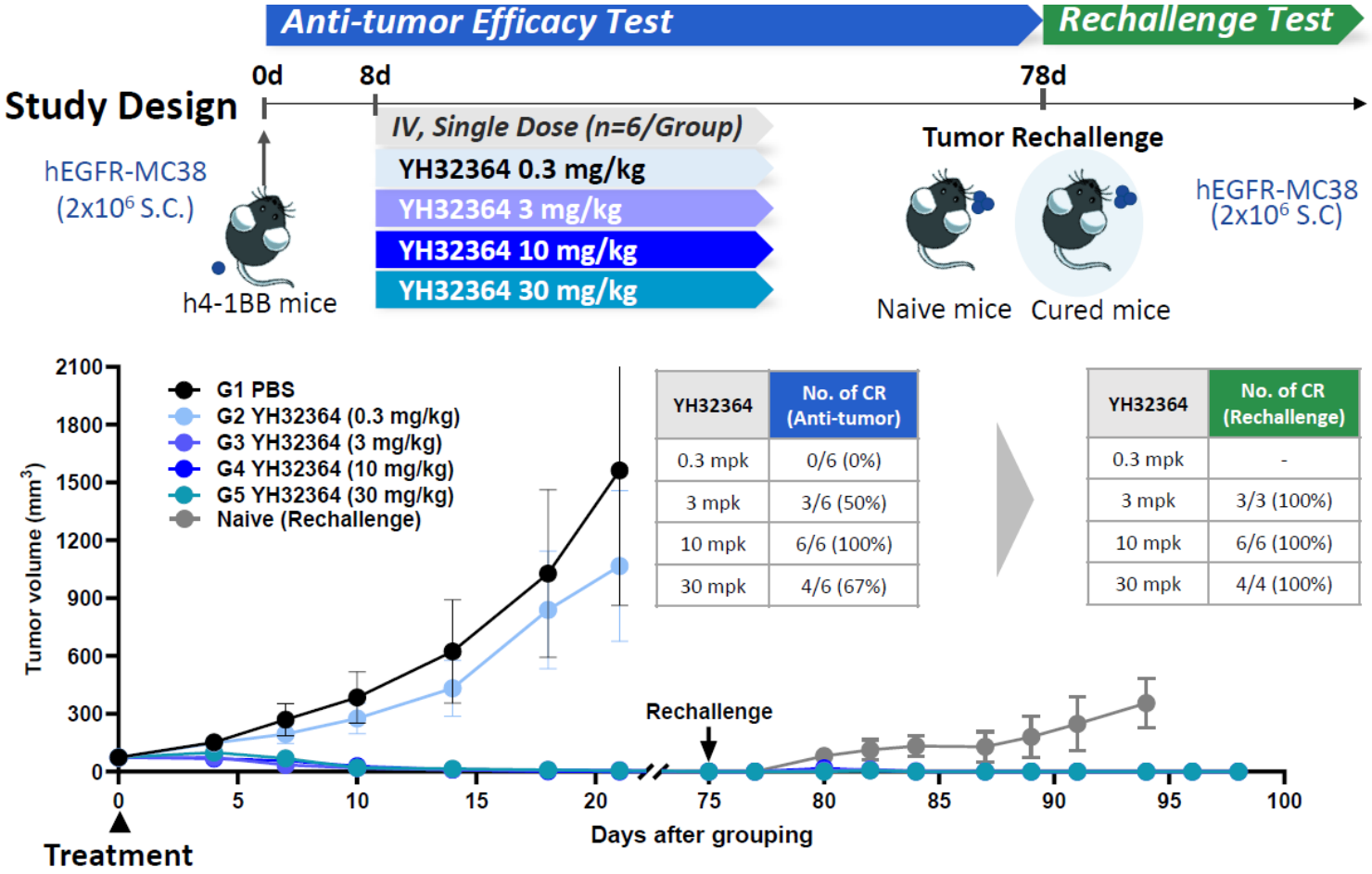
YH32364 shows a potent anti-tumor effect in mice



- Tumor: hEGFR-MC38/Mouse: h4-1BB KI (C57BL/6)
- Dosing regimen: IP, BIW
- Data is shown as Mean±SEM (n=5/group)
- ****; p<0.0001 vs hIgG1 / One-way ANOVA with Tukey post-hoc
- Urelumab: in house preparation

Fig. 5. *In vivo* efficacy in hEGFR-MC38 bearing 4-1BB KI mice

Single injection of YH32364 showed prolonged tumor suppression in rechallenge study



YH32364	No. of CR (Anti-tumor)
0.3 mpk	0/6 (0%)
3 mpk	3/6 (50%)
10 mpk	6/6 (100%)
30 mpk	4/6 (67%)

YH32364	No. of CR (Rechallenge)
0.3 mpk	-
3 mpk	3/3 (100%)
10 mpk	6/6 (100%)
30 mpk	4/4 (100%)

Fig. 6. Immune memory by YH32364 treatment confers durable TGI

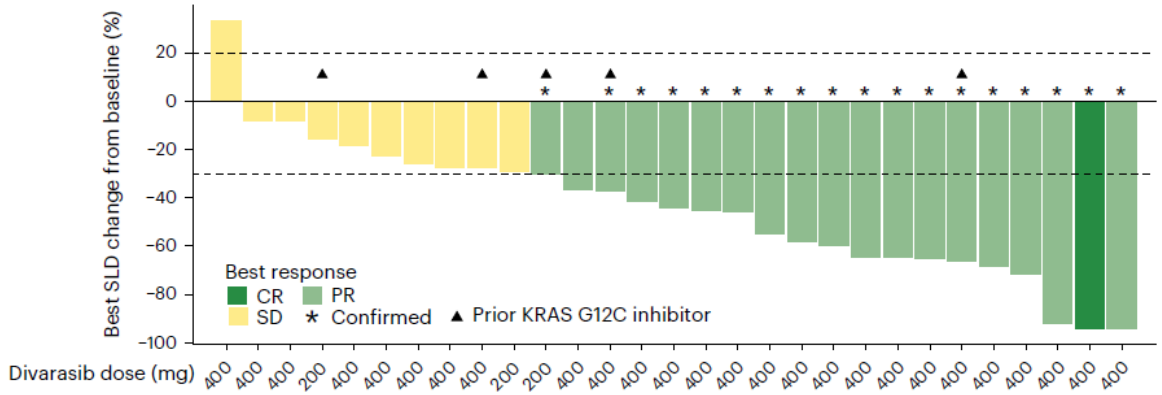
CRC: Divarasib+Cetuximab clinical trial from Roche

nature medicine

Article

https://doi.org/10.1038/s41591-023-02696-8

Divarasib plus cetuximab in *KRAS G12C*-positive colorectal cancer: a phase 1b trial



Combination and NCT#	Phase	Population	N	Efficacy
Cetuximab+Divarasib NCT04449874	**1b**	**Advanced or metastatic CRC**	**29**	**Previous G12C inhibition (n=5) ORR: 60% G12C inhibition naive (n=24) ORR: 62.5% mPFS: 8.1m**

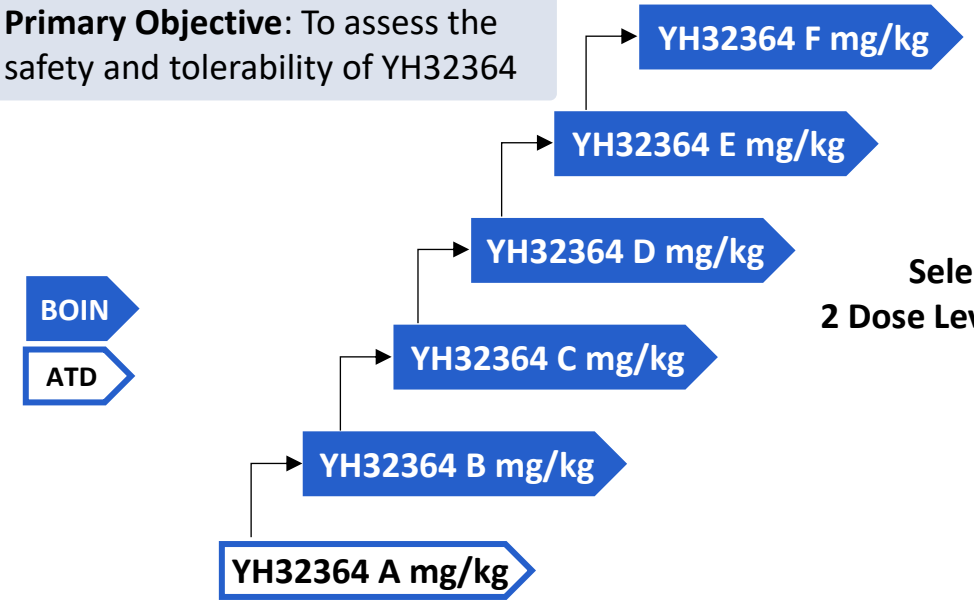
Roche's Investor Update (AACR2023, Phase 1b study)

- Combination of Divarasib and Cetuximab demonstrated, **ORR of 62% with manageable safety profile** in advanced colorectal cancer with KRAS G12C inhibitor

YH32364-101 First-in-human Study Design

Part 1 Dose Escalation
(Locally advanced or metastatic EGFR overexpressing solid tumors)

Primary Objective: To assess the safety and tolerability of YH32364

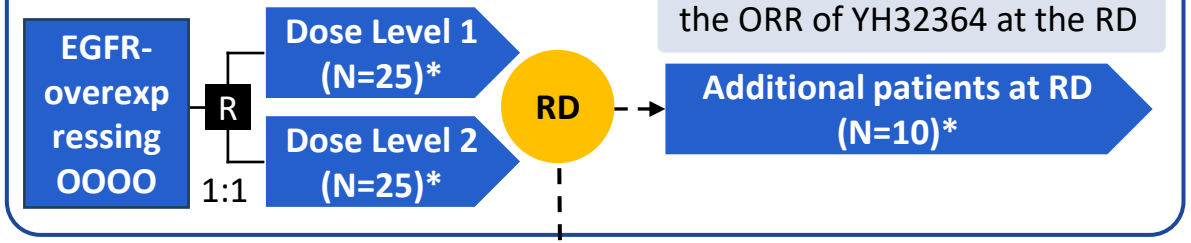


Selection of 2 Dose Levels for Part 2

Part 2 Dose Expansion

Dose Optimization (Cohort 1)

Primary Objective: To assess the ORR of YH32364 at the RD



Cohort 2

EGFR overexpressing solid tumor type A** (N=35)

5604 : Antitumor activity of YH42946, a potent tyrosine kinase inhibitor, in NSCLC harboring EGFR exon 20 insertion mutations

Mi Ra Yu[1†], Jii Bum Lee[2†], Kwangho Lee[3†], Min Hee Hong[4], Sun Min Lim[4*], Byoung Chul Cho[4**]

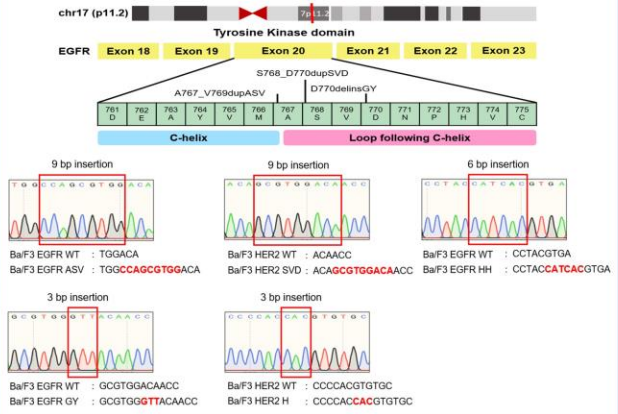
[1] Yonsei New Il Han Institute for Integrative Lung Cancer Research, Yonsei University College of Medicine, Seoul, Republic of Korea, [2] Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea
[3] Bio & Drug Discovery Division, Korea Research Institute of Chemical Technology, Daejeon 34114, Republic of Korea, [4] Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

BACKGROUD

Epidermal growth factor receptor (EGFR) mutations are the most common in non-small cell lung cancer (NSCLC) patients, with around 30% carrying these mutations, of which approximately 4–10% are EGFR exon 20 insertion (ex20ins) mutations. The most common EGFR ex20ins mutations in NSCLC are ASV and SVD variants in the kinase domain. Currently, treatment options for this subset of patients are limited. YH42946 is an orally available tyrosine kinase inhibitor (TKI) targeting EGFR ex20ins mutations, and the potential to be a best-in-class drug candidate to address this unmet clinical need.

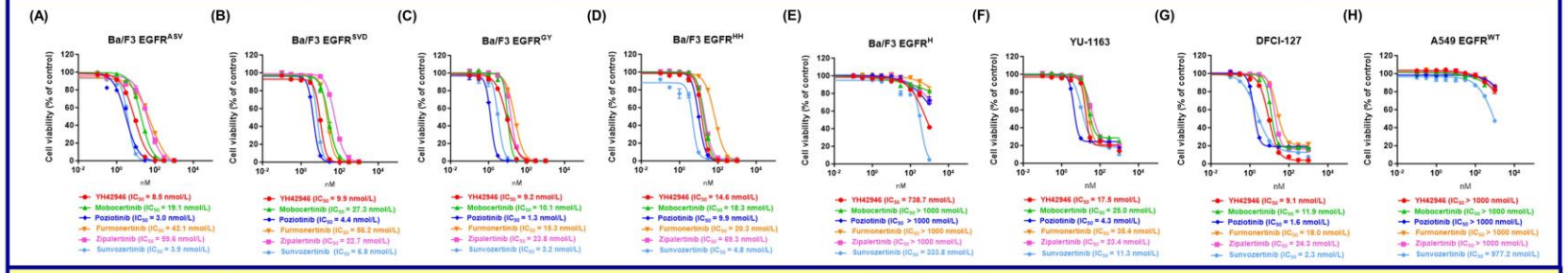
METHODS

Competitive binding affinity was measured using the KINOMEscan® screening platform. The inhibitory activity of YH42946 was evaluated through a cell viability assay in Ba/F3 cell lines expressing EGFR ASV, SVD, GY, and HH mutations. A549 cells were used to assess the cellular activity of EGFR wild-type (WT). To further confirm the mechanism of action, western blot analysis was performed on patient-derived cells (PDCs), including YU-1163 (S768_D770dup, SVD) and DFCI-127 (P772_H773insPNP).

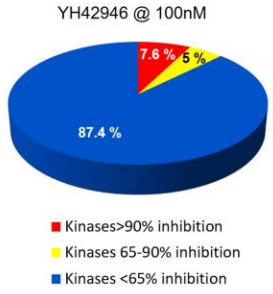


IN-VITRO EFFICACY

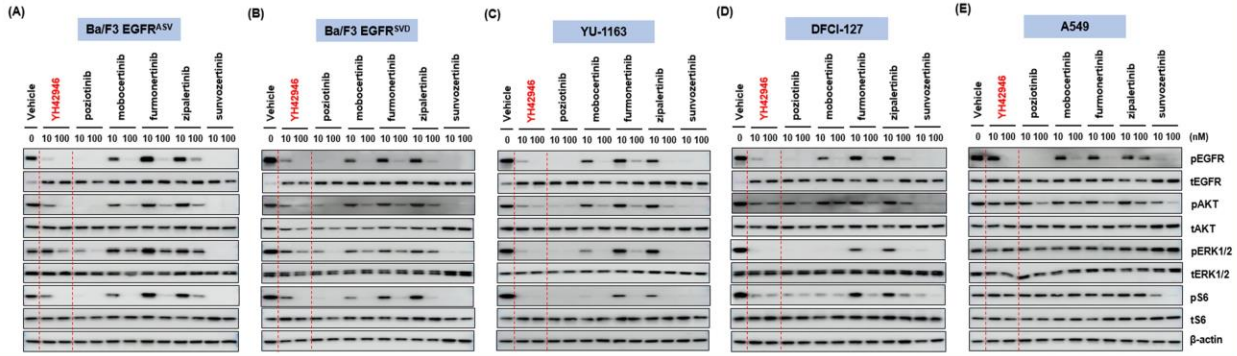
Cell proliferation



Kinase activity



Signaling pathway



CONCLUSIONS

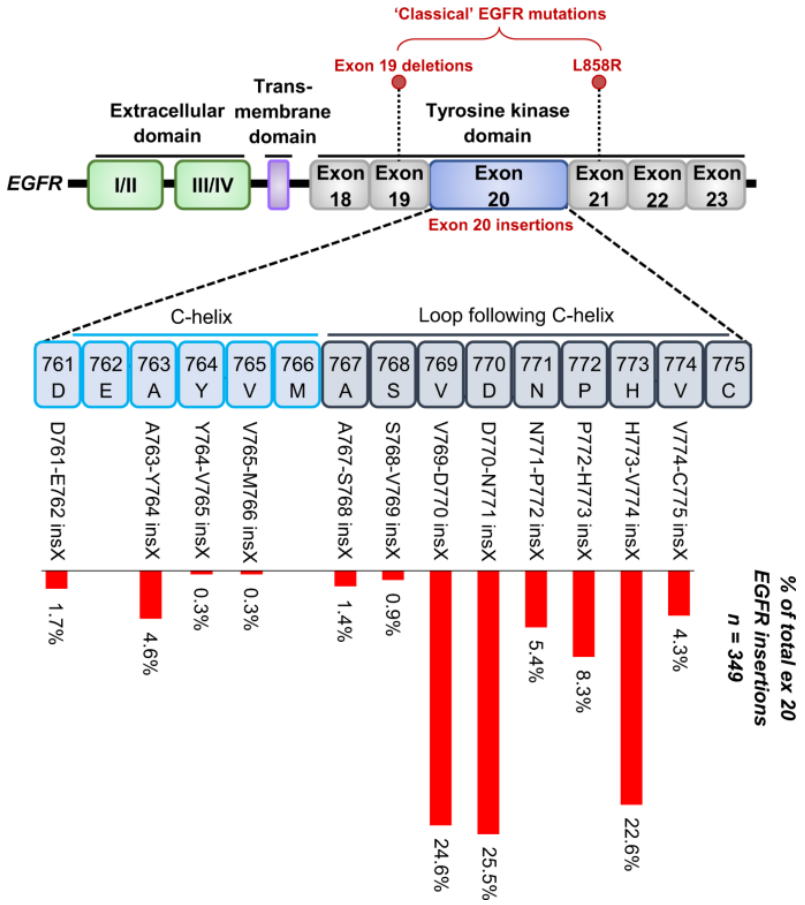
YH42946 is a potent small-molecule inhibitor that selectively targets EGFR ex20ins while sparing EGFR WT in preclinical models, offering potential therapeutic benefits for NSCLC patients with EGFR ex20ins mutations. Additionally, YH42946 has demonstrated effective inhibition of the EGFR pathway. Given these robust activities against EGFR ex20ins, YH42946 is anticipated to provide a significant therapeutic option for NSCLC patients harboring EGFR ex20ins mutations.

Presented at IASLC 2025 AACR, April 25-30, 2025. Please contact cbc1971@yuhs.ac, mira0802@yuhs.ac for permission to reprint and/or distribute.

References: 1. Baraibar, I., Mezquita, L., Gil-Bazo, I., & Planchard, D. (2020). Novel drugs targeting EGFR and HER2 exon 20 mutations in metastatic NSCLC. Critical Reviews in Oncology/Hematology, 148, 102906.
Disclosures: This research was funded by YUHAN Company. YUHAN Company reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content.

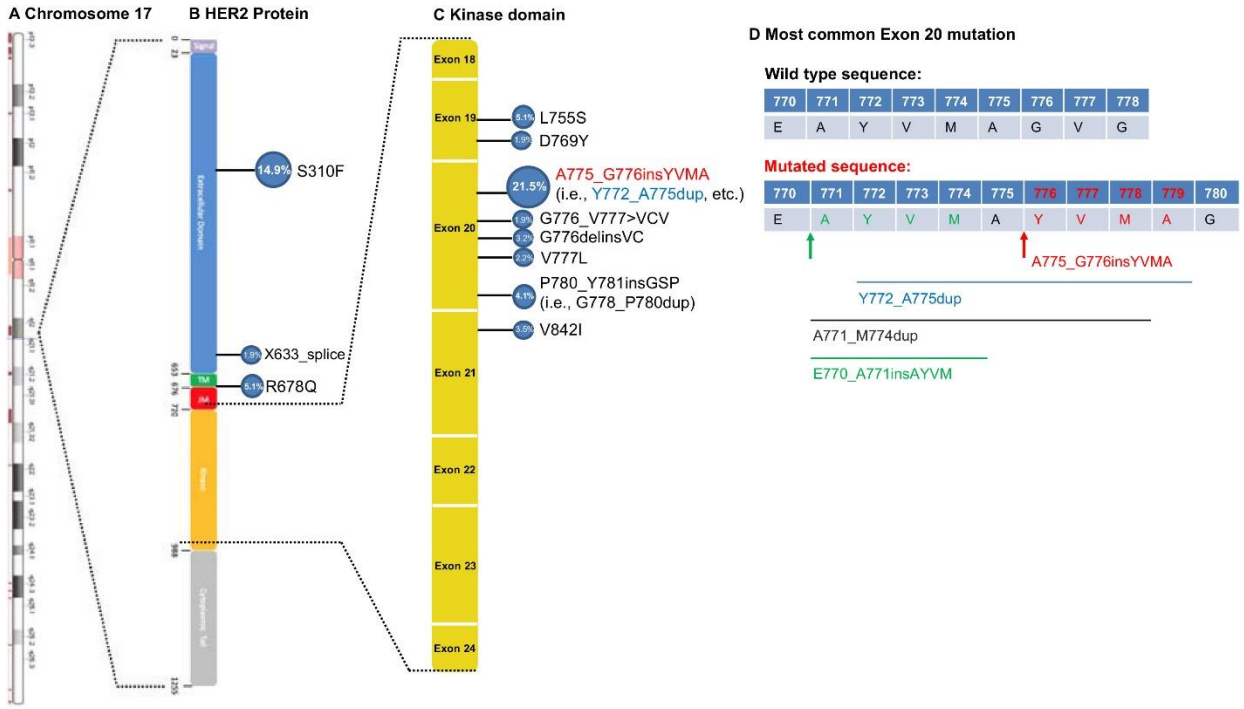
EGFR and Her2 exon 20 mutation in NSCLC

EGFR exon20 mutation: 0.3-3.7%



https://www.nature.com/articles/s41392-019-0038-9

Her2 exon20 mutation: 2-4%



https://doi.org/10.1016/j.jncc.2021.04.001

https://doi.org/10.1016/j.critrevonc.2020.102906

A Phase 1/2, Open-Label, Multicenter, First-in-Human Study to Evaluate the Safety, Pharmacokinetics, and Anti-Tumor Activity of YH32367 in Patients With HER2+ Locally Advanced/ Metastatic Solid Tumors

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CONCLUSIONS

- The HER2 × 4-1BB bispecific antibody YH32367, at doses ≤30 mg/kg, showed favorable safety, promising clinical benefit, especially in BTC, and a nonlinear PK profile in previously treated patients with HER2+ locally advanced or metastatic solid tumors, supporting further development in the dose-optimization phase
- The 3 mg/kg and 6 mg/kg doses of YH32367, both given every 3 weeks, were selected for dose optimization based on safety, efficacy, PK, biomarker, and model-based analyses

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DISCLOSURES

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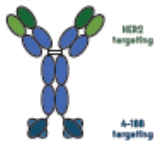
INTRODUCTION

- Dysregulation/overexpression of human epidermal growth factor receptor 2 (HER2), a member of the receptor tyrosine kinase family, is associated with the development of many types of human cancers, including breast, gastric, and biliary tract cancers (BTCs)[1-3]
- HER2-targeted therapies have improved patient outcomes; however, new treatment options are needed to address acquired resistance to anti-HER2 therapies and disease progression[4]
  - Combining HER2-targeted therapy with immunotherapy, specifically 4-1BB (TNFRSF9, CD137), a member of the tumor necrosis factor receptor superfamily and costimulator of immune cells, may improve clinical outcomes for patients with solid cancers after disease progression[4-6]
- YH32367 is a HER2/4-1BB–targeting bispecific antibody engineered by linking each C-terminus of an anti-HER2 antibody to a 4-1BB–binding single-chain variable fragment to target HER2 and amplify tumor-localized superagonist activity of 4-1BB while minimizing off-target toxicity (Figure 1)
  - In preclinical studies, YH32367 demonstrated potent anti-tumor and long-term immune memory effects, likely through tumor-directed T-cell activation[7,8]

Figure 1. Structure of YH32367



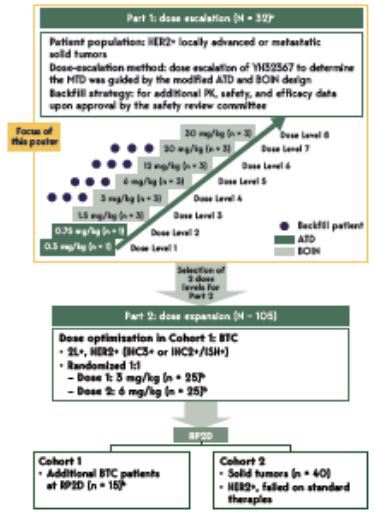
OBJECTIVE

- We report dose-escalation results from Part 1 of a 2-part, phase 1/2 study evaluating the safety, pharmacokinetics (PK), and anti-tumor activity of YH32367 in patients with HER2+ locally advanced or metastatic solid tumors

METHODS

- Patients with HER2+ (immunohistochemistry [IHC]3+ or IHC2+/in situ hybridization [ISH]+) locally advanced or metastatic solid tumors that were refractory or intolerant to standard therapy received intravenous YH32367 on Day 1 of 21-day cycles across 8 dose levels (0.3-30 mg/kg; Figure 2)
  - HER2 expression had to be confirmed in tumor tissue samples collected after prior HER2 therapy for the patients who received prior HER2-targeted therapy
- The primary endpoint was safety
- Key secondary endpoints reported here include PK, objective response rate (ORR), disease control rate (DCR), and duration of response (DoR); response was assessed by the investigator

Figure 2. Trial Design



RESULTS

Study Population

- At the data cutoff (May 24, 2024), 32 patients had been enrolled across 8 dose levels (Table 1)
  - The median age was 60 years (range, 34-79), and 63% of patients were male
  - The most common type of cancer was BTC (14 [44%]), followed by gastric cancer (9 [28%])
  - The median (range) number of prior treatment lines was 2 (0-7), with a median (range) number of prior trastuzumab-based regimens of 1 (0-3)

Table 1. Baseline Demographic and Clinical Characteristics

	0.3 mg/kg (n = 1)	0.75 mg/kg (n = 1)	1.5 mg/kg (n = 3)	3 mg/kg (n = 6)	6 mg/kg (n = 6)	12 mg/kg (n = 6)	20 mg/kg (n = 6)	30 mg/kg (n = 3)	Total (N = 32)
Median (range) age, y	53	55	67 (66-74)	57 (49-75)	60 (50-71)	57 (49-77)	62 (53-70)	61 (34-79)	60 (34-79)
Male, n (%)	1 (100)	1 (100)	1 (33)	4 (67)	4 (67)	4 (67)	3 (50)	2 (67)	20 (63)
Race, n (%)									
Asian	1 (100)	1 (100)	3 (100)	6 (100)	6 (100)	4 (67)	5 (83)	3 (100)	29 (91)
White	0	0	0	0	0	2 (33)	1 (17)	0	3 (9)
ECOG PS score, n (%)									
0	1 (100)	0	1 (33)	3 (50)	3 (50)	2 (33)	2 (33)	3 (100)	15 (47)
1	0	1 (100)	2 (67)	3 (50)	3 (50)	4 (67)	4 (67)	0	17 (53)
Type of cancer, n (%)									
BTC*	0	1 (100)	3 (100)	2 (33)	4 (67)	2 (33)	0	2 (67)	14 (44)
Gastric	1 (100)	0	0	1 (17)	2 (33)	2 (33)	3 (50)	0	9 (28)
Salivary gland	0	0	0	2 (33)	0	0	0	1 (33)	3 (9)
Breast	0	0	0	0	0	0	2 (33)	0	2 (6)
NSCLC	0	0	0	1 (17)	0	0	1 (17)	0	2 (6)
Other†	0	0	0	0	0	2 (33)	0	0	2 (6)
HER2 expression, n (%)									
IHC3+ and ISH+	0	0	0	0	1 (17)	1 (17)	0	0	2 (6)
IHC3+ and ND	1 (100)	1 (100)	1 (33)	5 (83)	4 (67)	4 (67)	4 (67)	2 (67)	22 (69)
IHC2+ and ISH+	0	0	2 (67)	1 (17)	1 (17)	1 (17)	2 (33)	1 (33)	8 (25)
Prior treatment lines, median (range)	4.0 (4.0-4.0)	2.0 (2.0-2.0)	1.0 (1.0-3.0)	1.5 (1.0-5.0)	2.5 (1.0-4.0)	1.5 (0-3.0)	4.0 (1.0-7.0)	2.0 (2.0-3.0)	2.0 (0-7.0)
Prior trastuzumab-based regimens,‡ median (range)	3.0 (3.0-3.0)	0	0	0.5 (0-3.0)	0 (0-2.0)	0.5 (0-1.0)	2.0 (0-3.0)	2.0 (1.0-2.0)	1.0 (0-3.0)

ATD, antibody-drug conjugate; BTC, biliary tract cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; NE, not done; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.
*Includes intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder cancer, and ampullary adenocarcinoma.
†Includes colon cancer and vaginal cancer.
‡Includes trastuzumab, trastuzumab ADC, trastuzumab in combination with pertuzumab, nazbitrastat, nazbitrastat ADC, HI-specific antibody containing anti-HER2. 4 patients received prior HER2 TKIs; 2 patients received prior tucatinib in combination with trastuzumab; 2 patients (both in the 30 mg/kg group) received prior lapatinib in combination with chemotherapy (capecitabine) and were excluded from the results shown in this row.

Safety

- No dose-limiting toxicities were observed; maximum tolerated dose was not reached
- Treatment-emergent adverse events (TEAEs) occurred in 25/32 (78%) patients; grade ≥3 TEAEs occurred in 6 (19%) patients (Table 2)
- Treatment-related adverse events (TRAEs) occurred in 10 (31%) patients; grade ≥3 TRAEs occurred in 1 (3%) patient (Table 2)
  - The most commonly reported TRAEs were pyrexia (5 [16%]) and chills (4 [13%])
  - No significant dose dependency was observed in TRAEs
  - 1 TRAE led to death (ejection fraction decreased, 0.75 mg/kg) due to investigator-assessed disease progression as the primary cause, with decreased ejection fraction contributing, likely resulting from disease progression or sepsis based on the clinical course
- Adverse events classified as infusion-related reactions, related to cytokine release syndrome, and immune related were reported in 4 (13%), 4 (13%), and 1 (3%) patients, respectively (Table 2)
- Dose interruptions due to TEAEs were reported in 4 (13%) patients, and no patients reported TEAEs leading to dose reduction or withdrawal (Table 2)

Table 2. Safety Summary

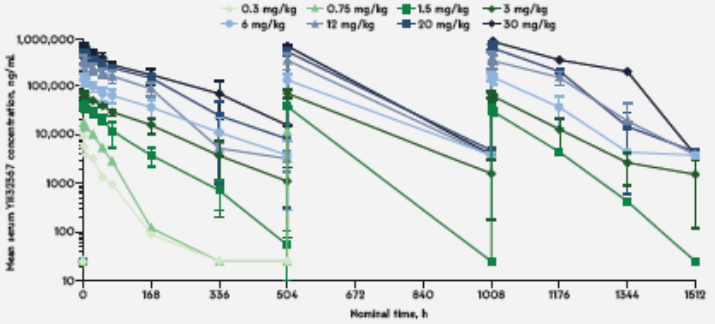
	0.3 mg/kg (n = 1)	0.75 mg/kg (n = 1)	1.5 mg/kg (n = 3)	3 mg/kg (n = 6)	6 mg/kg (n = 6)	12 mg/kg (n = 6)	20 mg/kg (n = 6)	30 mg/kg (n = 3)	Total (N = 32)
TEAE, n (%)	0	1 (100)	2 (67)	4 (67)	5 (83)	6 (100)	4 (67)	3 (100)	25 (78)
Grade ≥3 TEAE	0	1 (100)	0	0	1 (17)	1 (17)	1 (17)	2 (67)	6 (19)
Serious TEAE	0	1 (100)	0	0	1 (17)	2 (33)	0	1 (33)	5 (16)
TRAE, n (%)	0	1 (100)	2 (67)	3 (50)	1 (17)	3 (50)	0	0	10 (31)
Grade ≥3 TRAE	0	1 (100)	0	0	0	0	0	0	1 (3)
Serious TRAE	0	1 (100)	0	0	0	0	0	0	1 (3)
TEAE leading to death, n (%)	0	1 (100)	0	0	0	0	0	0	1 (3)
TEAE leading to dose interruptions, n (%)	0	0	1 (33)	1 (17)	1 (17)	1 (17)	0	0	4 (13)
TRAEs by PT, n (%)									
Pyrexia	0	0	1 (33)	2 (33)	1 (17)	1 (17)	0	0	5 (16)
Chills	0	0	0	2 (33)	1 (17)	1 (17)	0	0	4 (13)
Fatigue	0	0	0	0	0	1 (17)	0	0	1 (3)
Alanine aminotransferase increased	0	0	0	0	1 (17)	0	0	0	1 (3)
Aspartate aminotransferase increased	0	0	0	0	1 (17)	0	0	0	1 (3)
Ejection fraction decreased	0	1 (100)	0	0	0	0	0	0	1 (3)
Hyalgia	0	0	0	0	1 (17)	0	0	0	1 (3)
Peripheral sensory neuropathy	0	0	0	1 (17)	0	0	0	0	1 (3)
Palmar-plantar erythrodysesthesia syndrome	0	0	0	0	0	1 (17)	0	0	1 (3)
Rash	0	0	1 (33)	0	0	0	0	0	1 (3)
AE classification, n (%)									
IRR	0	0	0	2 (33)	1 (17)	1 (17)	0	0	4 (13)
CRS	0	0	0	1 (17)	2 (33)	1 (17)	0	0	4 (13)
IrAE	0	0	1 (33)	0	0	0	0	0	1 (3)

AE, adverse event; CRS, cytokine release syndrome; IrAE, immune related adverse event; IRR, infusion related reaction; PT, preferred term; TEAE, treatment-emergent adverse event; TRAE, treatment related adverse event.

PK

- PK exposure increased slightly greater than dose proportionally, attributable to target-mediated drug disposition (Figure 3)

Figure 3. Mean Serum Concentration-Time Profiles of YH32367: Cycle 1 Day 1 Predose (0 Hours) to Cycle 4 Day 1 Predose (0 Hours)



Efficacy

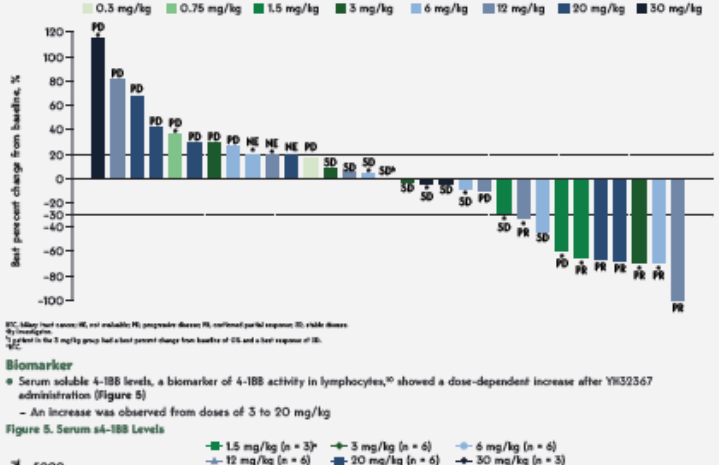
- Confirmed ORR was 23% and confirmed DCR was 56%; median DoR was not reached (NR; 95% confidence interval [CI], 4.2-NR; Table 3)
  - In patients with BTC, confirmed ORR was 31% and confirmed DCR was 62%; median DoR was NR (95% CI, 8.3-NR)
- An analysis of investigator-assessed percent change from baseline in the sum of target lesion diameters supported the DCR results, with 17/31 patients demonstrating stable disease or better (Figure 4)

Table 3. Efficacy Summary*

	0.3 mg/kg	0.75 mg/kg	1.5 mg/kg	3 mg/kg	6 mg/kg	12 mg/kg	20 mg/kg	30 mg/kg	Total
Overall population	n = 1	n = 1	n = 3	n = 5	n = 6	n = 6	n = 6	n = 3	N = 31
ORR,† n (%)	0	0	1 (33)	1 (20)	1 (17)	2 (33)	2 (33)	0	7 (23)
DCR,‡ n (%)	0	0	2 (67)	4 (80)	4 (67)	3 (50)	2 (33)	2 (67)	17 (55)
Median (95% CI) DoR,§ mo	–	–	NR	8.3 [NR-NR]	NR	4.2 [NR-NR]	NR	–	NR (4.2-NR)
BTC subgroup	n = 0	n = 1	n = 3	n = 1	n = 4	n = 2	n = 0	n = 2	n = 13
ORR,† n (%)	0	0	1 (33)	1 (100)	1 (25)	1 (50)	0	0	4 (31)
DCR,‡ n (%)	0	0	2 (67)	1 (100)	3 (75)	1 (50)	0	1 (50)	8 (62)
Median (95% CI) DoR,§ mo	–	–	NR	8.3 [NR-NR]	NR	NR	–	–	NR (8.3-NR)

BTC, biliary tract cancer; CI, confidence interval; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response; SD, stable disease.
*Percentages are based on the number of patients in the response evaluable population.
†ORR was defined as confirmed complete response + confirmed PR.
‡DCR was defined as confirmed complete response + confirmed PR + SD.
§DoR was defined as the time from the date of first documented response (that was subsequently confirmed) until the date of documented progression or death, whichever came first.

Figure 4. Waterfall Plot of Best Percent Change From Baseline in Sum of Target Lesion Diameters*

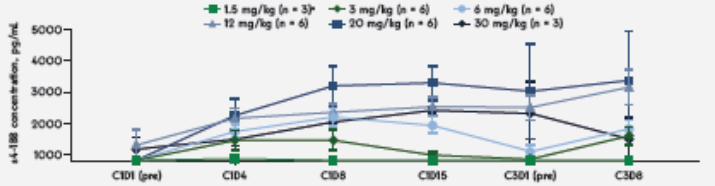


BTC, biliary tract cancer; NE, not evaluable; PR, progressive disease; PR, confirmed partial response; SD, stable disease.
*By investigator.
†A patient in the 3 mg/kg group had a best percent change from baseline of -11% and a best response of SD.
‡BTC.

Biomarker

- Serum soluble 4-1BB levels, a biomarker of 4-1BB activity in lymphocytes,[10] showed a dose-dependent increase after YH32367 administration (Figure 5)
  - An increase was observed from doses of 3 to 20 mg/kg

Figure 5. Serum s4-1BB Levels



C, Cycle; D, Day; LLOQ, lower limit of quantification; pre, predose; s4-1BB, soluble 4-1BB.
*Serum s4-1BB levels were below the quantitative limit of the analysis method (LLOQ: 750 pg/mL).