2024
HLB
IR

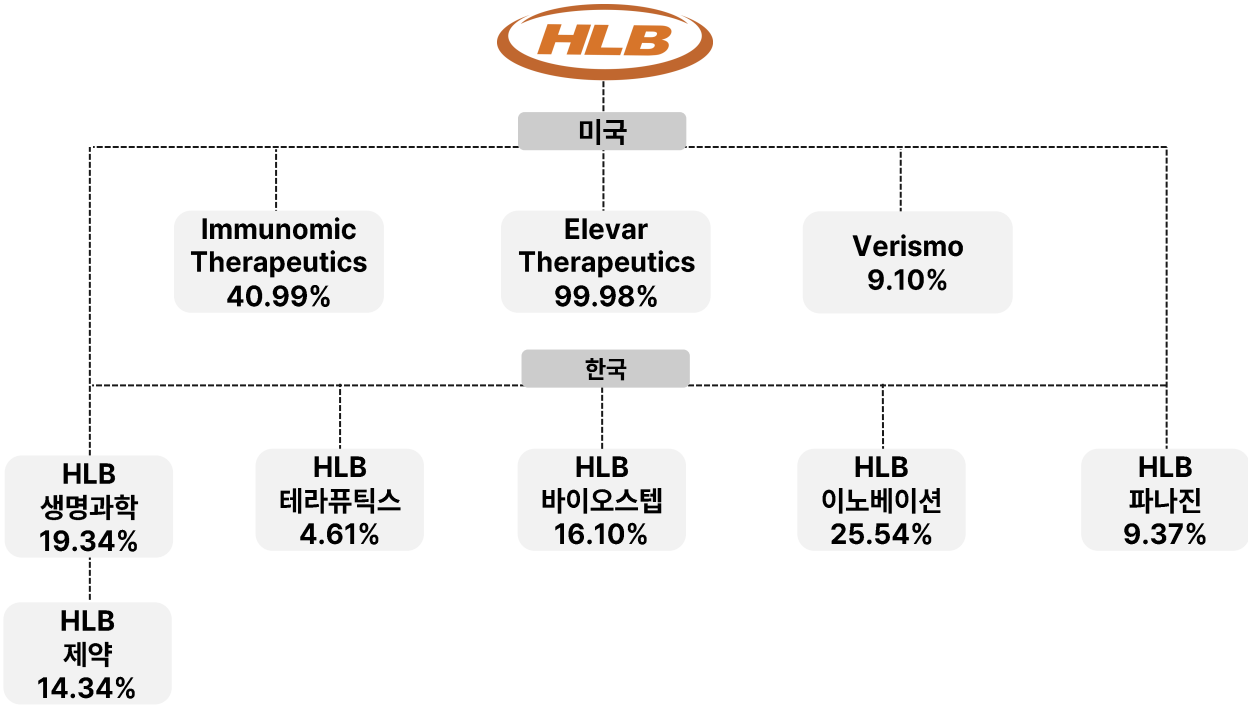
HLB 글로벌투자전략팀

회사 개요

회사 요약

대표이사	진양곤, 백윤기
임직원 수	199명
사업내용	바이오・헬스케어
본점소재지	세종특별자치시
자본금 (2023 3Q)	645 억원
자산 (2023 3Q)	1조 1,100 억원
매출 (2023 3Q)	223 억원
상장시장	KOSDAQ
시가총액 (2024.01.16)	5조 6,833억원

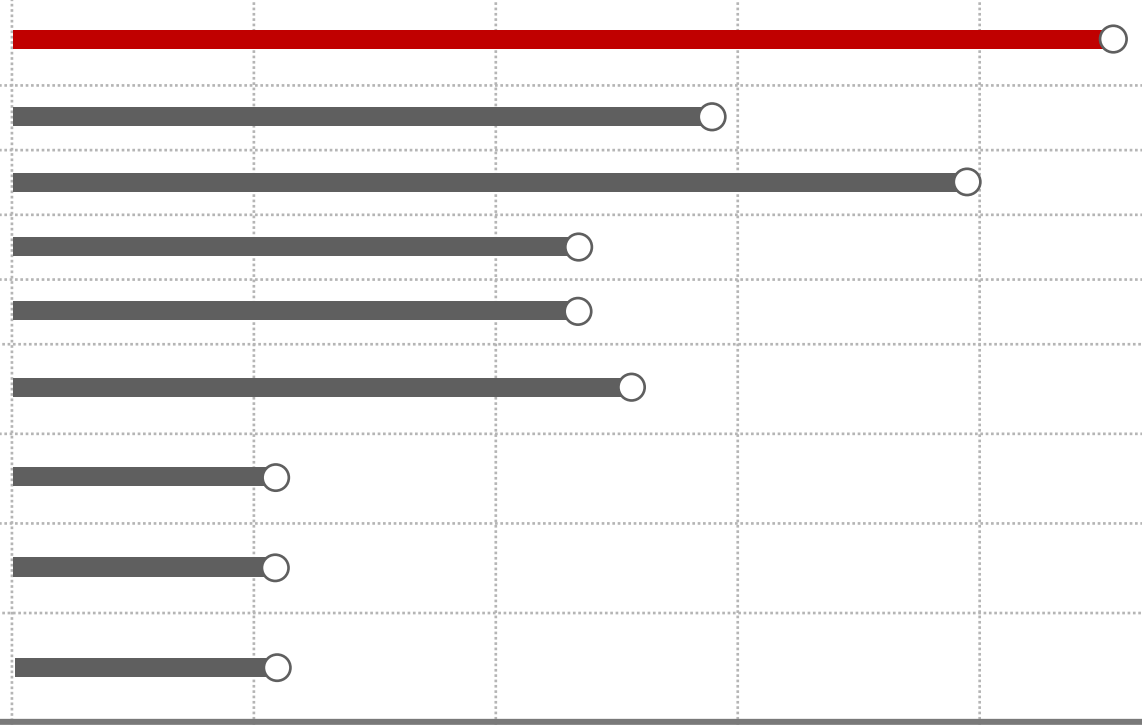
HLB 계열사 구조



출처: 2023년 9월 분기보고서 및 KRX 정보데이터시스템

주요 파이프라인

회사명	적응증	권리	단독/병용	임상진행 상황
				전임상 / 1상 / 2상 / 3상 / NDA
Elevar Therapeutics	간암 (HCC) 1차	글로벌 (중국제외)	Rivoceranib + Camrelizumab 병용	
	선낭암 (ACC) 1차		Rivoceranib 단독	
	위암 3/4차		Rivoceranib 단독	
	위암 2차		Paclitaxel 병용	
	대장암 3차		Lonsurf 병용	
Immunomic Therapeutics	교모세포종 (ITI-1000)	글로벌	Dendritic Cell vaccine	
	교모세포종 (ITI-1001)		DNA vaccine	
	메르켈세포암 (ITI-3000)		DNA vaccine	
Verismo Therapeutics	고형암 (SynKIR-110)	글로벌	CAR-T 치료제	



출처: Global Liver Cancer Drugs Strategic Market Report to 2030 by Yahoo finance, Feb. 11, 2023

주요 파이프라인 임상데이터

	간암 1차	선낭암 1차	위암 3차	교모세포종 (ITI-1000)
	(리보세라닙)			
임상단계	• 글로벌 임상 3상 완료 • FDA NDA 심사중	• 글로벌 임상 2상 종료 • FDA NDA 신청 준비중	• 글로벌 임상 3상 종료 • data 분석 완료 및 NDA 준비중	• 미국 임상 2상 • 현재 data 수집 및 분석 중
피험자 수	543 명	80 명	460 명	175 명
프로토콜	• Randomized, 2-arm • Rivoceranib 250 mg QD + Camrelizumab 200 mg Q2W vs Sorafenib 400 mg BID	• Single-arm • Rivoceranib 700mg PO QD in 28 days cycles	• Randomized, Placebo • Rivoceranib 700mg PO QD • 28days cycle	• Randomized, 3-arm • Vaccine doses 4-10 on day 22-24 of each temozolomide cycle
임상 End Points	• Primary endpoints: mPFS, mOS • Secondary endpoints: ORR	• Primary endpoints: ORR • Secondary endpoints: DOR, PFS, TTP, OS	• Primary endpoints: mOS • Secondary endpoints: PFS, ORR, DCR	• Primary endpoints: mOS • Secondary endpoints: Change in IR, PFS

출처: Clinical Trials org.

간암1차 치료제 임상데이터 비교

약물	Rivoceranib + Camrelizumab	Atezolizumab + Bevacizumab	Tremelimumab + Durvalumab	Lenvatinib	Sorafenib
환자 수	**543명**	501명	782명	954명	602명
대조군	**Sorafenib**	Sorafenib	Sorafenib	Sorafenib (비열등성)	Placebo
OS	**22.1 vs. 15.2 HR 0.62**	19.2 vs 13.4 HR 0.66	16.4 vs 13.8 HR 0.78	13.6 vs 12.3 HR: 0.92	10.7 vs 7.9 HR: 0.69
PFS	**5.6 vs. 3.7 HR 0.52**	6.8 vs 4.3 HR 0.59	3.8 vs 4.1 HR 0.9	7.4 vs 3.7 HR: 0.66	5.5 vs 2.8
ORR	**25.4% vs. 5.9%**	27.3% vs 11.9%	20.1% vs 5.1%	18.8% vs 6.5%	2% vs 1%
DCR	**78.3% vs. 53.9%**		73.6% vs. 55.3%		43% vs 32%
시장 점유율	**50% 목표**	52%	25%		
비고	***NDA 심사중**	2020년 승인	2022년 승인	2018년 승인	2007년 승인

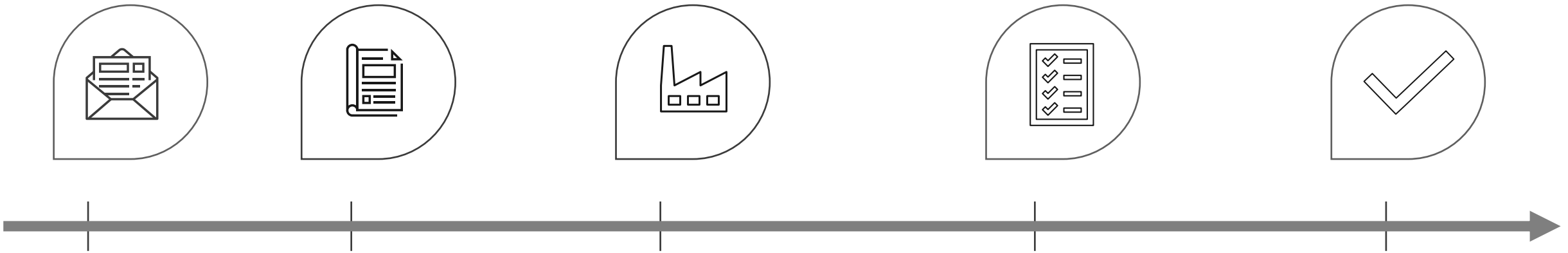
출처: Clinical Trail Gov.
*23년 5월 NDA 신청 → 7월 NDA 본심사 검토 → 24년 5월16일 전 승인 여부 결정

리보세라닙/캄렐리주맙 주요 현황

Drug	Combination	Indications	Approval date	Line
Rivoceranib	camrelizumab	1st-line unresectable or metastatic hepatocellular carcinoma	2023.02	1st
		Advanced hepatocellular carcinoma	2020.12	2nd
		Gastric adenocarcinoma or gastroesophageal junction adenocarcinoma	2014.12	3rd
Camrelizumab	Rivoceranib	1st-line unresectable or metastatic hepatocellular carcinoma	2023.02	1st
	cisplatin+paclitaxel	1st-line unresectable locally advanced/relapsed or metastatic esophageal squamous cell carcinoma	2021.12	1st
	cisplatin+gemcitabine	1st-line locally relapsed or metastatic nasopharyngeal carcinoma	2021.06	1st
		Relapsed and refractory classical Hodgkin lymphoma after at least two systematic therapies	2021.06	3rd
		Advanced nasopharyngeal carcinoma progressed after or intolerable to 2nd-line+ chemotherapy	2021.04	2nd
	carboplatin+paclitaxel	1st-line locally advanced/metastatic sq-NSCLC	2020.06	1st
		Locally advanced or metastatic esophageal adenocarcinoma progressed after or intolerable to 1st-line treatment	2020.06	1st
	pemetrexed+carboplatin	Unresectable locally advanced or metastatic EGFR-mut ALK-negative NSCLC	2020.06	1st
		Advanced hepatocellular carcinoma after sorafenib and/or oxaliplatin-containing chemotherapy treatments	2020.03	2nd

출처: 항서제약 공식 홈페이지

리보세라닙 NDA 진행 현황



2023. 05
- NDA 신청

2023.07
- NDA 본 심사 개시

2023. 11/12
- FDA Mid-Cycle Review 이슈 없이 **완료**
- 리보세라닙 현장 실사 **완료**

2024. 03
- Final Review 예정

2024. 05
- FDA NDA 승인 결과 발표

바이오텍 기업 비교 테이블

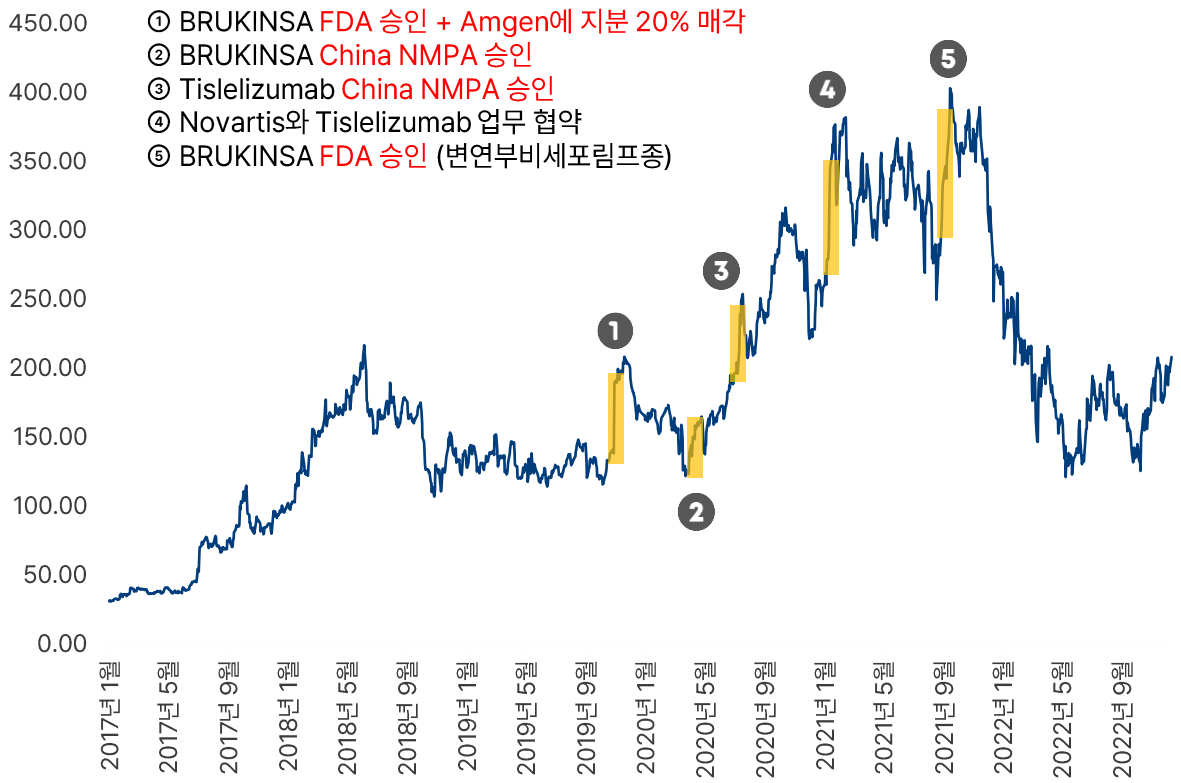
	HLB	BeiGene	Incyte	Eisai
설립일	10. 18, 1985	10. 28, 2010	04. 08, 1991	12.06, 1941
본사	서울, 한국	베이징, 중국 | 캠브릿지, 미국	윌밍턴, 미국	도쿄, 일본
IPO	KOSDAQ (KR)	NASDAQ (US), HKEX (HK), SSE (CH)	NASDAQ (US)	NiKKEI (Japan)
시가총액	5조 6,833억원	$19.9B (약 26조원)	$13.9B (약 18조원)	$14.2B (약 18조원)
주식 총 수	128,929,651	104,099,381	224,109,238	296,566,949
매출	223억원	$595.2mn	$954.6mn	3조7000억원
적응증	간암1차, 선낭암1차, 위암3차	외투세포림프종 (MCL) 월든스트롬 거시글로불혈증(WM)	골수섬유증, 다발성 경화증	갑상선암, 신장암, 간암, 자궁내막암, 유방암, 난소암, 쓸개관암, 알츠하이머, 불면증, 드라베 증후군
시장 규모	$13.3B	$10.05B	$3.0B	$27.2B

*매출, 주식총수 2023년 9월 말 기준, 시장 규모는 적응증 총합 규모, 시가총액 24년 1월16일 기준

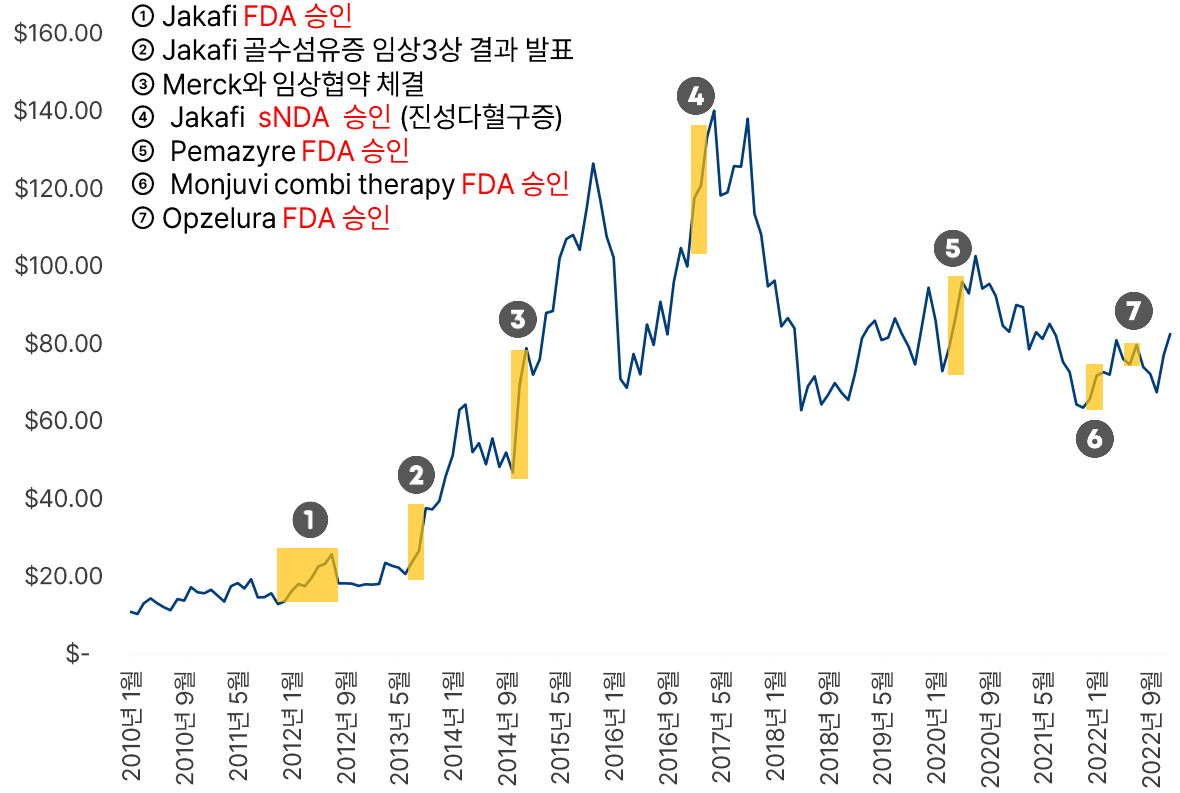
출처: 2023년 9월 분기보고서, Investing.com

주요 이벤트 타임라인 및 주가 추이

BeiGene



Incyte



출처: Investing.com 및 각사 공식홈페이지 IR섹션

간암1차 치료제 NDA승인이후 매출 추이

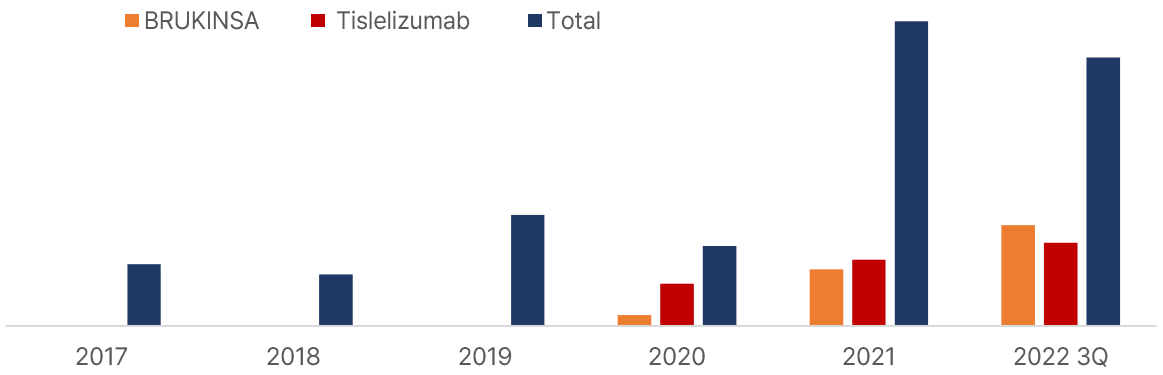
BeiGene

(in Thousands USD)

	BRUKINSA	Tislelizumab	Total
2017	-	-	$238,387
2018	-	-	$198,220
2019	$1,039	-	$428,212
2020	$41,702	$163,358	$308,874
2021	$217,987	$255,119	$1,176,283
2022	$564,651	$422,885	$1,254,612

BRUKINSA FDA Approval (2018)

Tislelizumab NMPA Approval (2019)

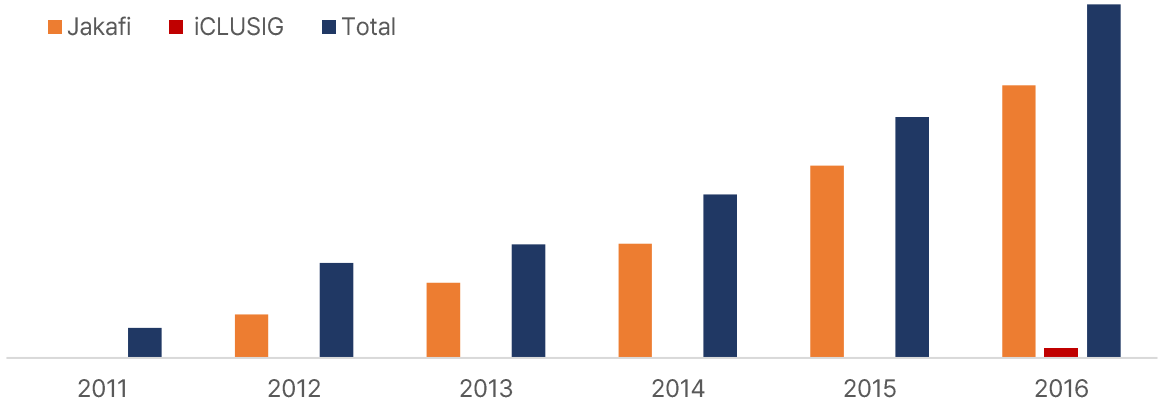


Incyte

(in Thousands USD)

	Jakafi	iCLUSIG	Total
2011	$2,012		$94,455
2012	$136,001	-	$297,059
2013	$235,443	-	$354,947
2014	$357,562	-	$511,495
2015	$601,015	-	$753,751
2016	$852,800	$29,600	$1,105,719

Jakafi FDA Approval (2011)



출처: Bloomberg

Eisai의 성장

주요 파이프라인

약물명	치료 분야	FDA 승인 시기	매출
Lenvima	갑상선암	Feb. 2015	1조 3,248억원
	신장암	May, 2016	
	간암	Aug, 2018	
	자궁내막암 (병용)	Sep, 2019	
	신장암 (병용)	Aug, 2021	
Dayvigo	신경계	Dec, 2019	1,696억원
Halaven	지방육종	Jan. 2016	1,644억원
Fycompa	신경계	Oct. 2012	1,189억원
Leqembi	신경계	Jan, 2023	*35억원

2023년 3월 Annual Report기준, 병용요법은 모두 머크의 키트루다와 함께 쓰임
*Leqembi 매출은 23년 1월 FDA승인 이후, 4월~9월달까지의 매출을 나타냄

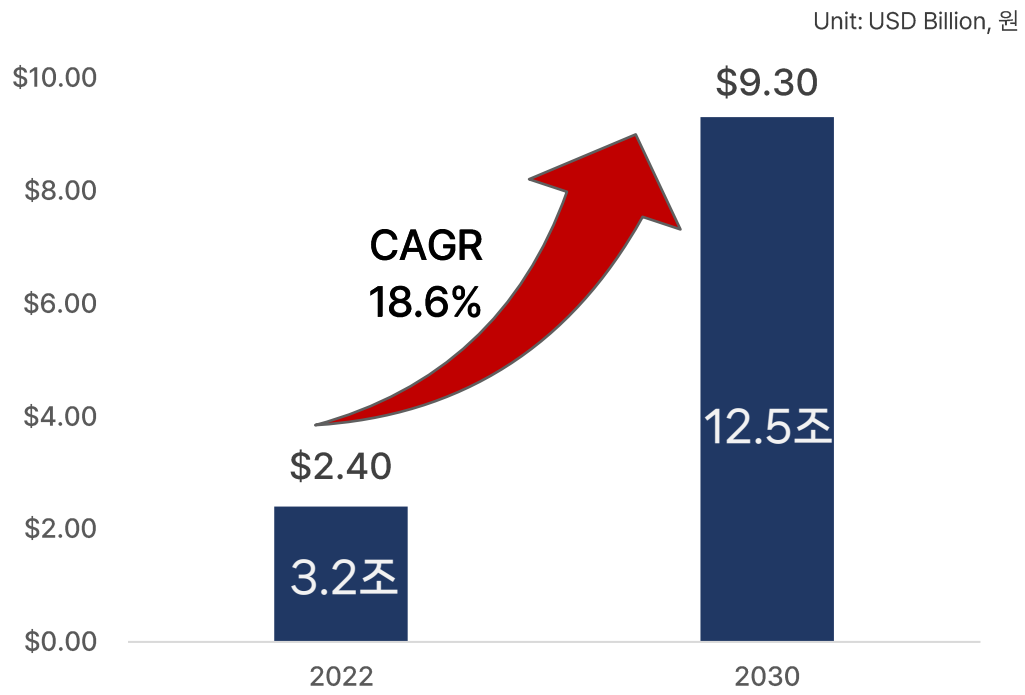
출처: Investing.com, Drugs.com

글로벌 간암 환자 수

출처: WHO, American Cancer Society, World Cancer Research Fund International, Digestive Cancers Europe, Clinical & Molecular Hepatology

간암1차치료제 시장 성장성

글로벌 간암 치료제 시장 규모

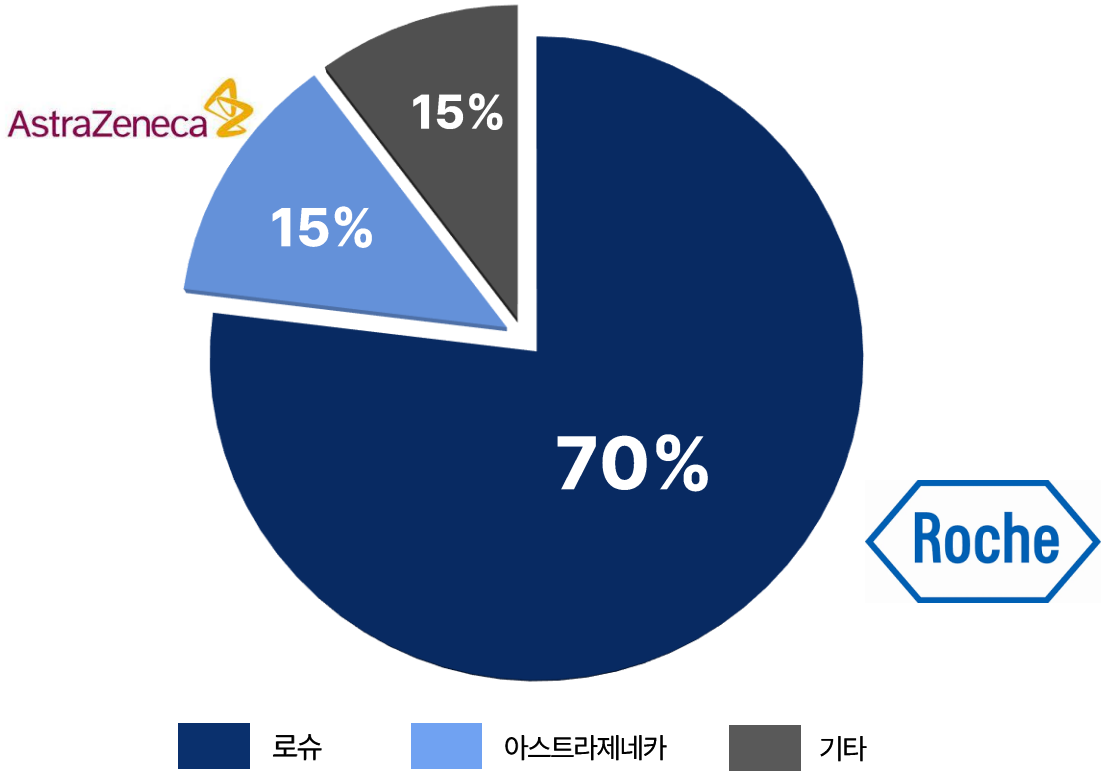


- ✓ 2022년 기준, 글로벌 간암시장 규모는 원화로 약 3.2조원
- ✓ 2030년 까지 연 18.6% 성장률로 12조원 규모로 성장할 것으로 예상
- ✓ HLB의 글로벌 목표시장점유율은 FDA승인 및 판매 후 2027년 까지 50%
  - 매출 3.1조 원 목표
  - 영업이익 2.6조 원 목표

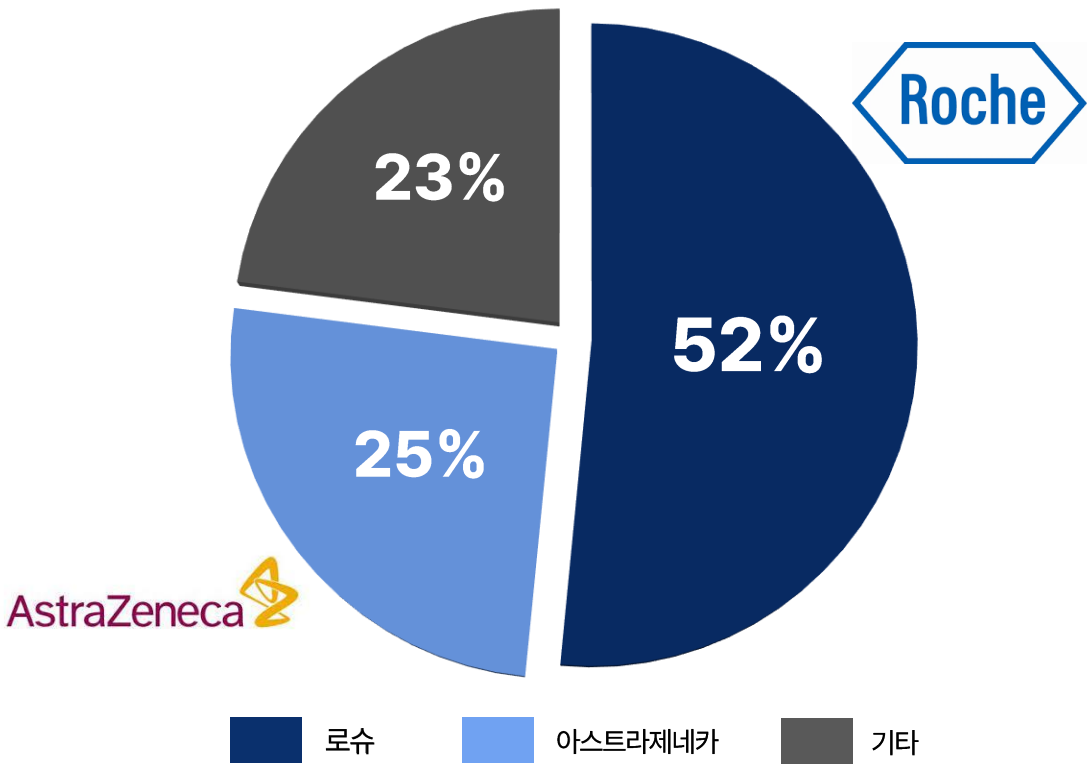
출처: Global Liver Cancer Drugs Strategic Market Report to 2030 by Yahoo finance, Feb. 11, 2023

간암1차 시장 경쟁사 점유율

23년 2월 말 기준



23년 11월 말 기준



출처: ElevarTx HCC Market Overview BrandImpact by IQVIA Oct, 2023

간암1차 치료제 NDA승인이후 매출 추이

Unit: USD Million

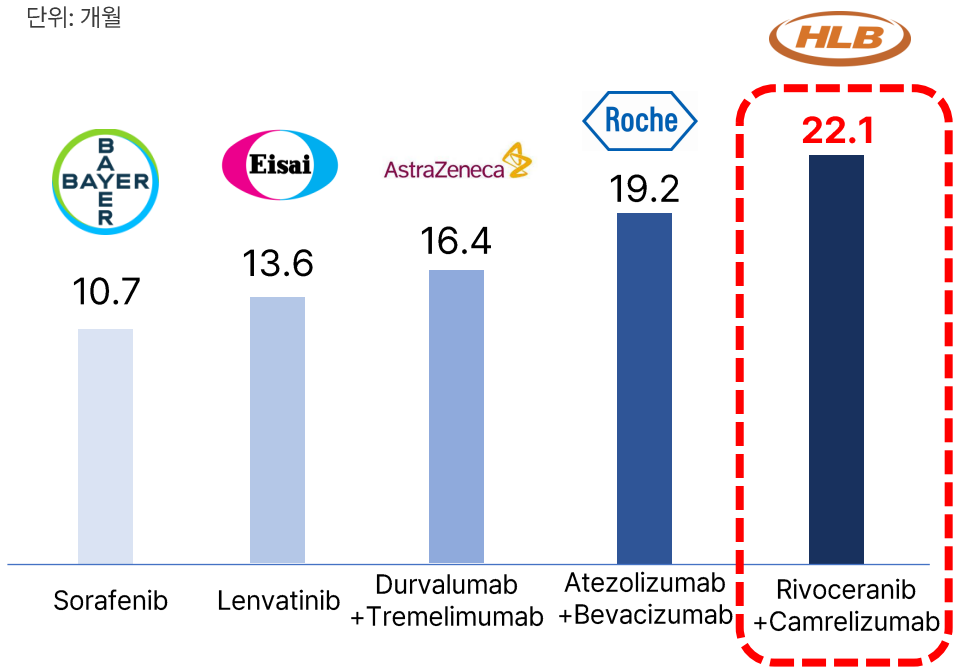
회사	약물	매출				
		2018	2019	2020	2021	2022
Roche	Avastin			5,319	3,343	2,321
	Tecentriq			2,919	4,326	3,894
AstraZeneca	Imfinzi					*2,784
	Imjudo					
Eisai	Lenvima	11.59	116.96	298.28	592.35	752.12
		2009	2010	2011	2012	
Bayer	Sorafenib	117.69	115.53	151.78	217.5	

AstraZeneca 2022년 Annual Report에 Imfinzi 매출에 Imjudo매출이 포함되어 있다 명시됨.

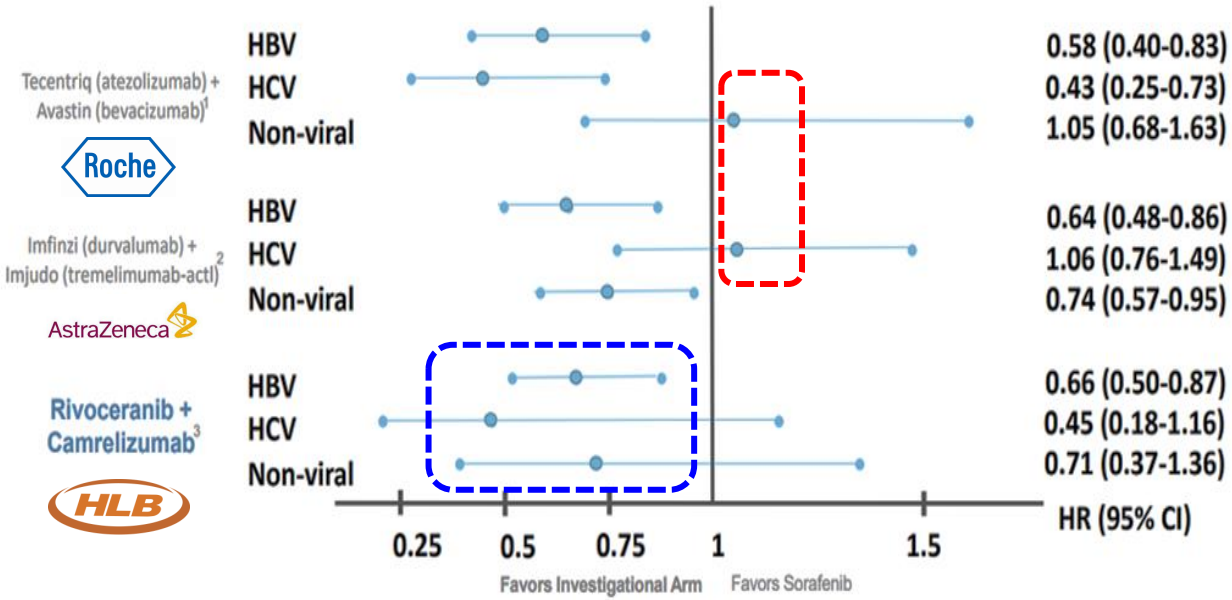
출처: Bloomberg, 각 사 10K form

Best-in-Class 임상데이터

간암 1차치료제 OS (생존 기간) 비교



간암 발병 인자 종류별 약효 비교



✓ 리보세라닙/캄렐리주맙, 현 간암1차치료제 중 역대 최장 생존기간 (OS) **22.1**개월을 기록

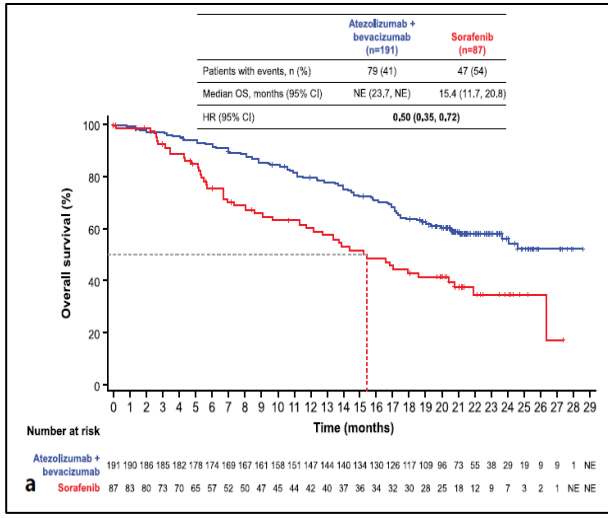
✓ 현 간암1차치료제 중 리보세라닙/캄렐리주맙이 유일하게 모든 발병원인 환자군에게 높은 약효가 입증됨

용어설명: OS (Overall Survival) = 생존 기간, HBV = B형간염, HCV = C형간염, Non-Viral = 비바이러스형

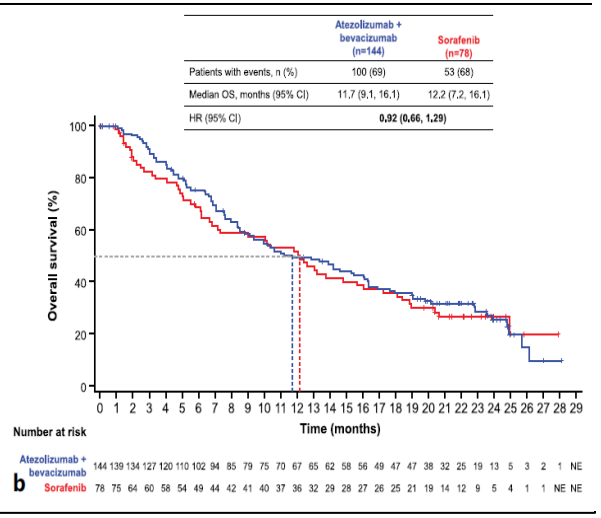
Best-in-Class 임상데이터

Imbrave-150 (Roche)
Atezolizumab (Tecentriq) + Bevacizumab (Avastin)

ALBI 1 Grade



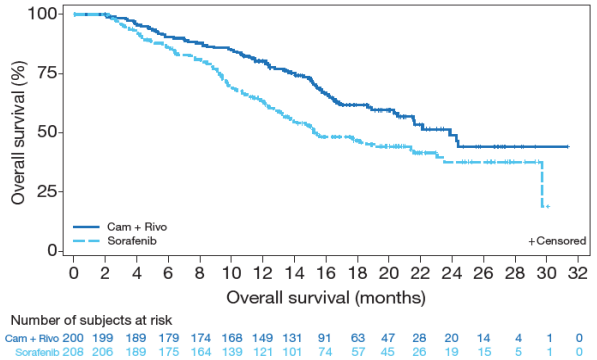
ALBI 2 Grade



- ✓ ALBI 1등급 환자에게만 약효가 좋으며 간기능이 안 좋은 환자들에게는 약효가 현저히 떨어짐
- ✓ ALBI G1 HR : 0.5 (0.35-0.72), ALBI G2 HR: **0.92 (0.66-1.29)

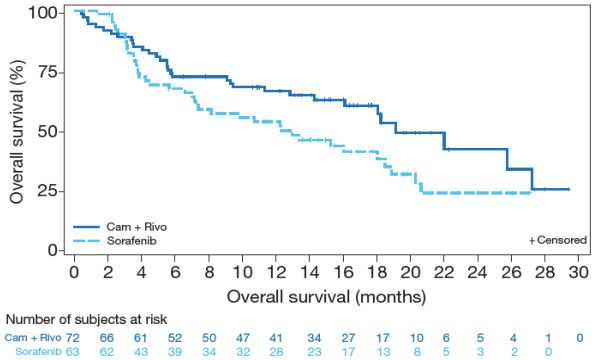
CARES-310 (HLB & Elevar)
Rivoceranib + Camrelizumab

ALBI 1 Grade



ALBI Grade 1	Cam + Rivo (n=200)	Sorafenib (n=208)
OS events, n (%)	78 (39.0)	112 (53.8)
Median OS,[a] months (95% CI)	23.9 (20.3, NE)	15.4 (13.3, 21.6)
Hazard ratio[b] (95% CI)	0.62 (0.47, 0.83)	

ALBI 2 Grade



ALBI Grade 2	Cam + Rivo (n=72)	Sorafenib (n=63)
OS events, n (%)	33 (45.8)	39 (61.9)
Median OS,[a] months (95% CI)	19.1 (14.3, 27.2)	12.3 (7.1, 18.5)
Hazard ratio[b] (95% CI)	0.62 (0.4, 1.0)	

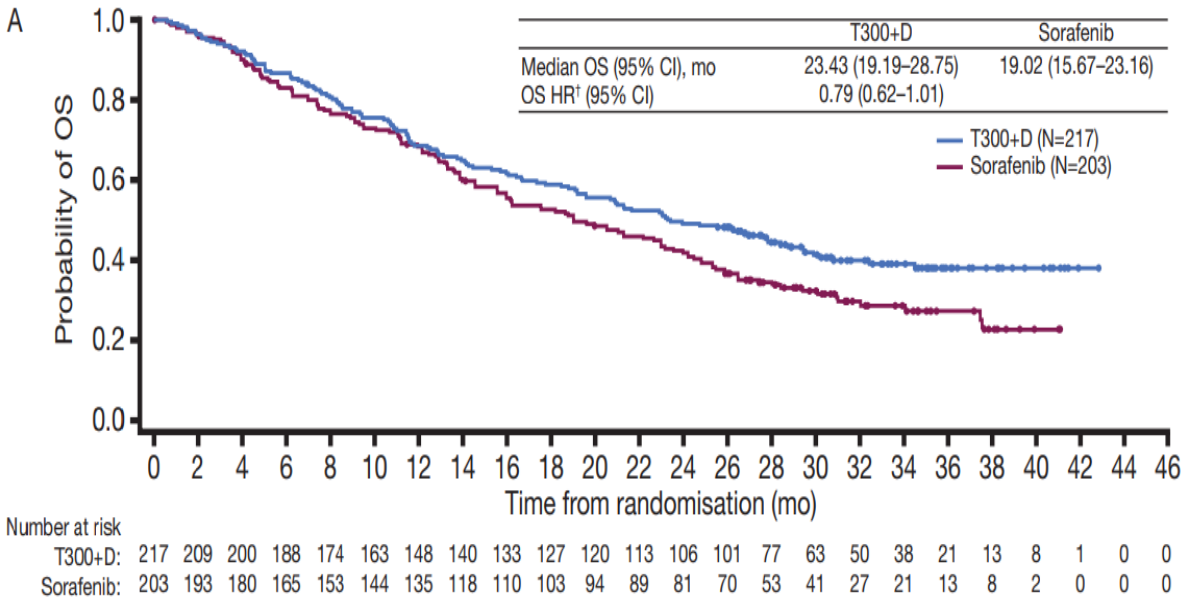
- ✓ ALBI 등급에 상관없이 모든 환자군에 약효가 좋으며 특히 Ate/Beva에서 약효가 없는 ALBI 2등급 환자들에게 우월한 약효를 나타냄
- ✓ ALBI G1 HR: 0.62 (0.47-0.83), ALBI G2 HR: 0.62 (0.4-1.0)

출처: Liver Cancer 2023, Supplementary appendix, Lancet 2023; published online July 24
*ALBI 1/2 Grade는 간 기능의 저하 능력을 나타내는 지표이며 Grade 2가 Grade 1보다 간 기능이 더 저하된 환자군임
**Hazard Ratio (HR)은 1에 가까울수록 약효가 없다는 뜻

Best-in-Class 임상데이터

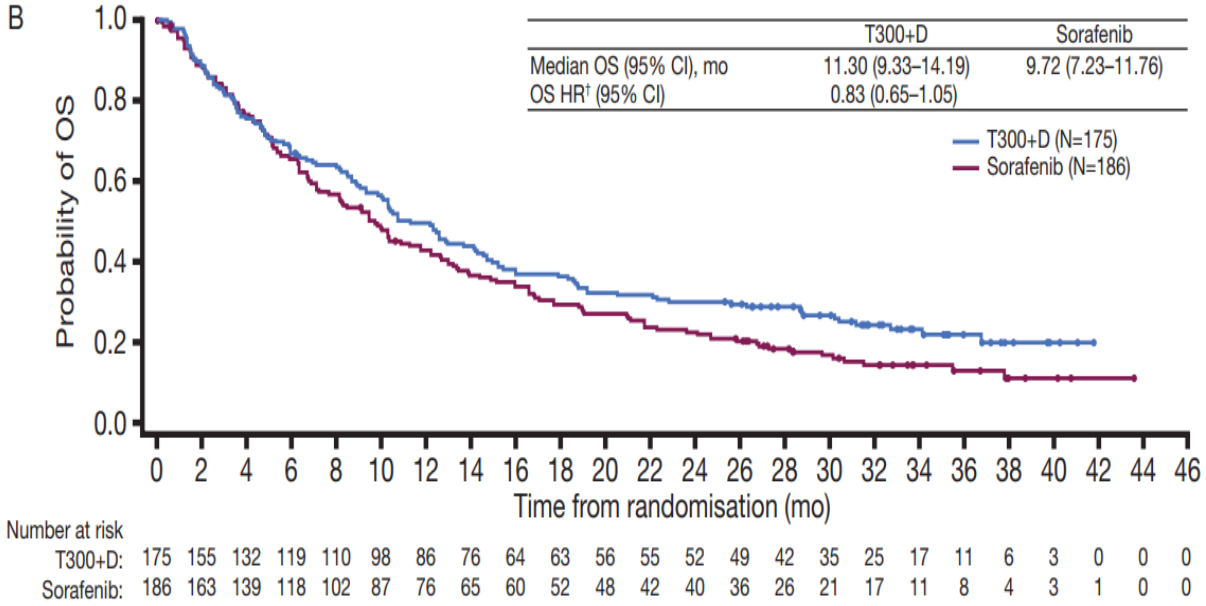
HIMALAYA (AstraZeneca)
Tremelimumab (Imjudo) + Durvalumab (Imfinzi)

ALBI 1 Grade



	T300+D	Sorafenib
Median OS (95% CI), mo	23.43 (19.19–28.75)	19.02 (15.67–23.16)
OS HR† (95% CI)	0.79 (0.62–1.01)	

ALBI 2 Grade

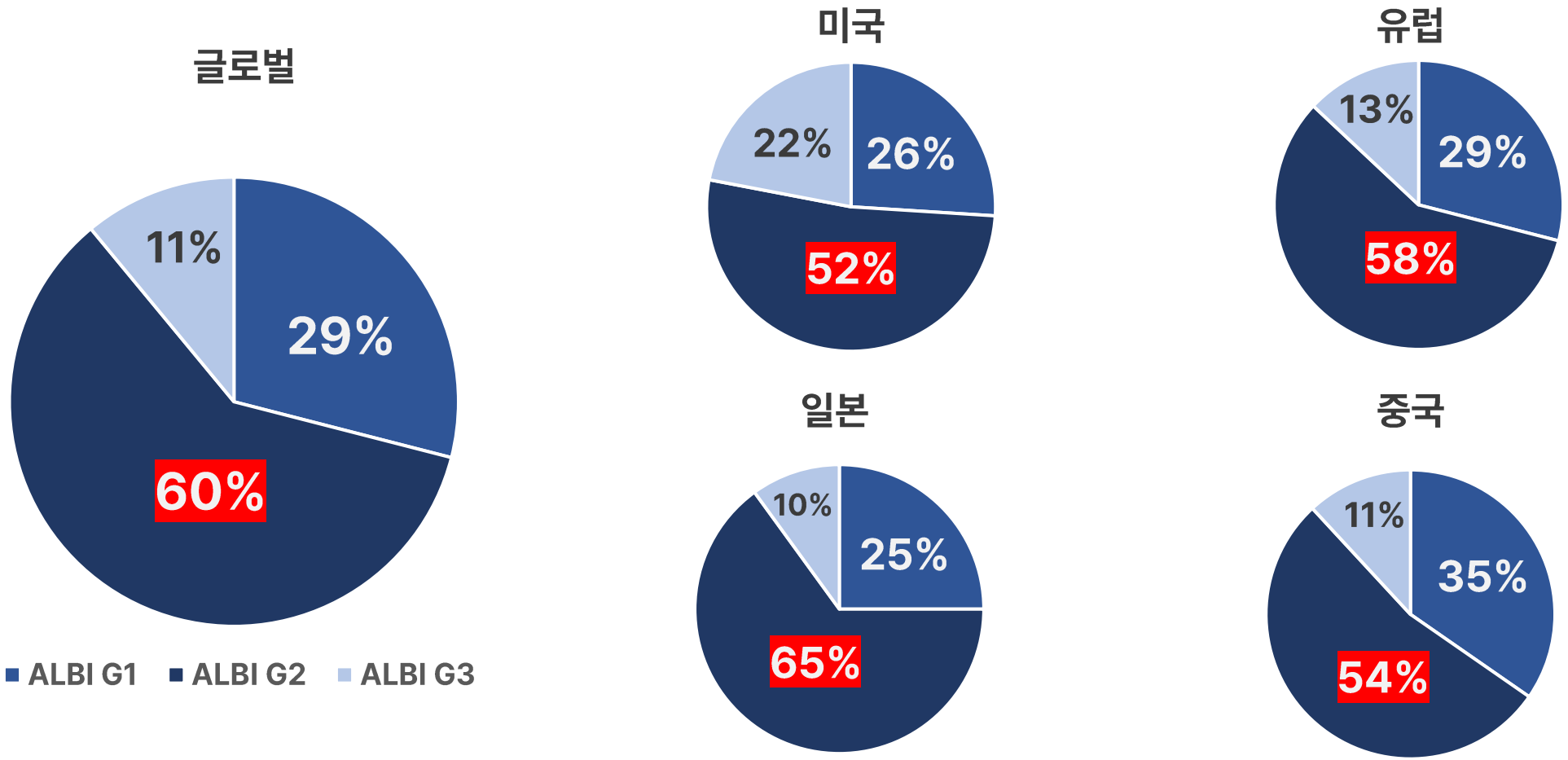


	T300+D	Sorafenib
Median OS (95% CI), mo	11.30 (9.33–14.19)	9.72 (7.23–11.76)
OS HR† (95% CI)	0.83 (0.65–1.05)	

✓ 아스트라제네카의 치료제는 ALBI Grade 2 환자에게 약효가 있지만, 당사의 치료제보다 OS가 약 **5.7개월** 낮아 경쟁력이 낮음

출처Abou-Alfa GK, et al. NEJM Evid Published online 6 June 2022. doi: 10.1056/EVIDoa2100070
*ALBI 1/2 Grade는 간 기능의 저하 능력을 나타내는 지표이며 Grade 2가 Grade 1보다 간 기능이 더 저하된 환자군임
**Hazard Ratio (HR)은 1에 가까울수록 약효가 없다는 뜻

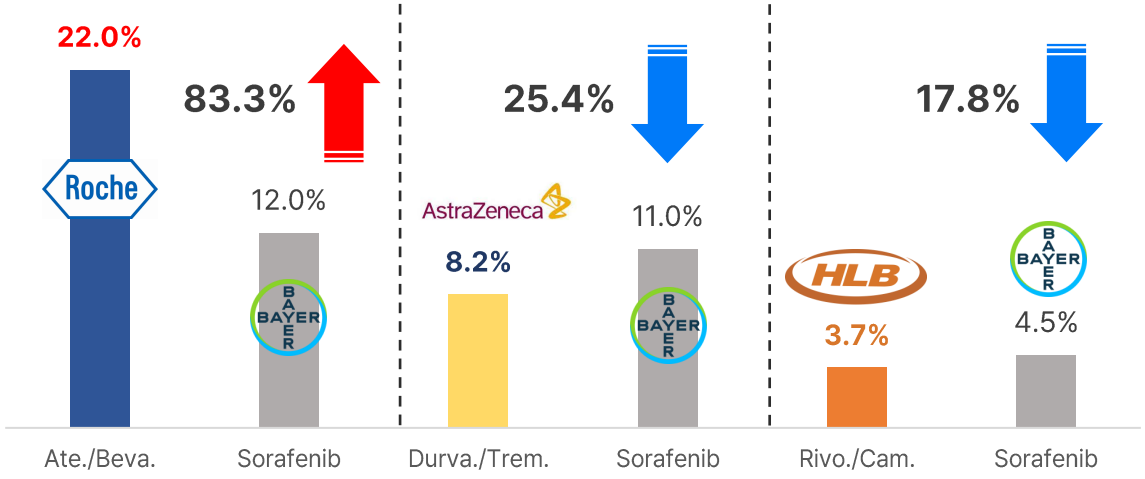
ALBI Grade 별 환자 수



출처:Karger.com/Albumin-Bilirubin Grade Analyses of Atezolizumab plus Bevacizumab versus Sorafenib in Patients with Unresectable Hepatocellular Carcinoma: A Post Hoc Analysis of the Phase III IMbrave150 Study

Best-in-Class 임상데이터

간암 1차 치료제 임상 중단율



간암1차 치료제 Half-Life 비교

치료제	약물 Half-Life
Sorafenib	25-48 hours
Lenvatinib	48 hours
Atezolizumab+Bevacizumab	20 days
Tremelimumab+Druvalumab	22 days
Rivcoceranib+Camrelizumab	11 hours

- ✓ 시장점유율이 가장 높은 Roche의 치료제가 대조군 대비 부작용으로 인한 임상중단율이 **83.3%**가 높음
- ✓ 아스트라제네카 대비 HLB는 **7.6%** 임상중단율을 보이지만 OS가 **34.8%** (5.7개월)이 길어 경쟁력 있음
- ✓ 현존 하는 간암1차치료제 중 리보세라닙/캄렐리주맙이 가장 낮은 약물 반감기를 가지고 있음
- ✓ 다른 약물과 달리 부작용 리스크가 적으며 약물 컨트롤이 용이 함

출처: JHEP Rep 2023 Feb 18;5(5):100702

Best-in-Class 임상데이터

향후 간암1차치료제 시장에서의 리보세라닙/캄렐리주맙 후행 약물

회사명	약물명	임상 NCT #	임상 단계	임상 종료 기간
Junshi Biosciences	Toripalimab	NCT04523493	3상	09.01.2026
AstraZeneca	Durvalumab	NCT03847428	3상	08.31.2025
BMS	Nivolumab+Relatlimab	NCT05337137	1/2상	12.15.2026
BMS	Nivolumab	NCT04039607	3상	06.30.2025
Merck	Pembrolizumab	NCT03867084	3상	08.31.2029
LG Chem+AstraZeneca	Tivozanib+Durvalumab	NCT03970616	1/2상	04.04.2023

✓ 향후 5년이내, 간암1차 치료제를 목표로 임상 중에 있는 약물 중 5년 내로 상업화가 될 가능성이 있는 약물은 없음

✓ 이 기간 동안 리보세라닙/캄렐리주맙의 매출을 극대화할 수 있으며 안정적인 시장점유율을 확보 할 수 있음

출처: Bloomberg, Clinical Trial Gov.

Best-in-Class 임상데이터

- ✓ 현재 리보세라닙/캄렐리주맙, 간암1차치료제 중 가장 높은 OS (Overall Survival) 생존기간 22.1개월 보유함
- ✓ 리보세라닙/캄렐리주맙은 타 경쟁사 치료제와 달리 간암 발병 인자와 상관없이 모든 환자군에 높은 약효가 입증 됨
- ✓ 간암1차치료제 시장에서 시장점유율이 가장 높은 Ate/Beva 치료제는 기저 ALBI 1등급 환자에게만 약효가 좋은 반면, 리보세라닙/캄렐리주맙은 기저 ALBI 1,2 등급 환자에게 모두 약효가 나타나며 특히, 경쟁사인 Ate/Beva에서 약효가 없는 ALBI 2등급 환자에게 월등히 좋은 약효가 나타남
- ✓ 리보세라닙/캄렐리주맙 , 간암1차 치료제 임상 중 임상중단율이 타 경쟁사 대비 현저히 낮았으며 (객관적 논문으로 재차 입증, 9페이지 참조) 부작용으로 인한 치료 중단 가능성이 매우 낮음
- ✓ 리보세라닙/캄렐리주맙, 약물 반감기가 타 경쟁사 대비 매우 짧은 약 11시간으로, 부작용 발생 시 약물 중단과 부작용 관리가 용이하며, 다른 치료제에 비해 부작용 리스크가 현저히 낮음

Lancet 논문 (발간일자: 07/24/2023)

Camrelizumab plus rivoceranib versus sorafenib as first-line therapy for unresectable hepatocellular carcinoma (CARES-310): a randomised, open-label, international phase 3 study

Shukui Qin, Stephen L Chan*, Shanzhi Gu, Yuxian Bai, Zhenggang Ren, Xiaoyan Lin, Zhendong Chen, Weidong Jia, Yongdong Jin, Yabing Guo, Xiaohua Hu, Zhiqiang Meng, Jun Liang, Ying Cheng, Jianping Xiong, Hong Ren, Fang Yang, Wei Li, Yajin Chen, Yong Zeng, Alexander Sultanbaev, Monika Pazgan-Simon, Margaryta Pisetska, Davide Melisi, Dmitriy Ponomarenko, Yurii Osypchuk, Ivan Sinielnikov, Tsai-Sheng Yang, Xiao Liang, Chunxia Chen, Linna Wang, Ann-Lii Cheng†, Ahmed Kaseb†, Arndt Vogel†, for the CARES-310 Study Group‡*

Summary

Background Immunotherapy with immune checkpoint inhibitors combined with an anti-angiogenic tyrosine-kinase inhibitor (TKI) has been shown to improve overall survival versus anti-angiogenic therapy alone in advanced solid tumours, but not in hepatocellular carcinoma. Therefore, a clinical study was conducted to compare the efficacy and safety of the anti-PD-1 antibody camrelizumab plus the VEGFR2-targeted TKI rivoceranib (also known as apatinib) versus sorafenib as first-line treatment for unresectable hepatocellular carcinoma.

Methods This randomised, open-label, international phase 3 trial (CARES-310) was done at 95 study sites across 13 countries and regions worldwide. Patients with unresectable or metastatic hepatocellular carcinoma who had not previously received any systemic treatment were randomly assigned (1:1) to receive either camrelizumab 200 mg intravenously every 2 weeks plus rivoceranib 250 mg orally once daily or sorafenib 400 mg orally twice daily. Randomisation was done via a centralised interactive response system. The primary endpoints were progression-free survival, as assessed by the blinded independent review committee per Response Evaluation Criteria in Solid Tumours version 1.1, and overall survival in the intention-to-treat population. Safety was assessed in all patients who received at least one dose of the study drugs. We report the findings from the prespecified primary analysis for progression-free survival and interim analysis for overall survival. This study is registered with ClinicalTrials.gov (NCT03764293).

Findings Between June 28, 2019, and March 24, 2021, 543 patients were randomly assigned to the camrelizumab–rivoceranib (n=272) or sorafenib (n=271) group. At the primary analysis for progression-free survival (May 10, 2021), median follow-up was 7·8 months (IQR 4·1–10·6). Median progression-free survival was significantly improved with camrelizumab–rivoceranib versus sorafenib (5·6 months [95% CI 5·5–6·3] *vs* 3·7 months [2·8–3·7]; hazard ratio [HR] 0·52 [95% CI 0·41–0·65]; one-sided p<0·0001). At the interim analysis for overall survival (Feb 8, 2022), median follow-up was 14·5 months (IQR 9·1–18·7). Median overall survival was significantly extended with camrelizumab–rivoceranib versus sorafenib (22·1 months [95% CI 19·1–27·2] *vs* 15·2 months [13·0–18·5]; HR 0·62 [95% CI 0·49–0·80]; one-sided p<0·0001). The most common grade 3 or 4 treatment-related adverse events were hypertension (102 [38%] of 272 patients in the camrelizumab–rivoceranib group *vs* 40 [15%] of 269 patients in the sorafenib group), palmar-plantar erythrodysaesthesia syndrome (33 [12%] *vs* 41 [15%]), increased aspartate aminotransferase (45 [17%] *vs* 14 [5%]), and increased alanine aminotransferase (35 [13%] *vs* eight [3%]). Treatment-related serious adverse events were reported in 66 (24%) patients in the camrelizumab–rivoceranib group and 16 (6%) in the sorafenib group. Treatment-related death occurred in two patients: one patient in the camrelizumab–rivoceranib group (ie, multiple organ dysfunction syndrome) and one patient in the sorafenib group (ie, respiratory failure and circulatory collapse).

Interpretation Camrelizumab plus rivoceranib showed a statistically significant and clinically meaningful benefit in progression-free survival and overall survival compared with sorafenib for patients with unresectable hepatocellular carcinoma, presenting as a new and effective first-line treatment option for this population.

Funding Jiangsu Hengrui Pharmaceuticals and Elevar Therapeutics.

글로벌 간암 학계 KOL의 평가

✓ "리보세라닙+캄렐리주맙 병용요법은 간암분야에서 가장 긴 환자생존율을 보였으며 1차 치료제의 새로운 옵션을 제시한다"

by Ghassan K. Abou-Alfa 교수

(미국 Memorial Sloan Kettering Cnacer Center)

✓ "리보세라닙과 캄렐리주맙 병용요법은 간암 1차 치료제의 높은 효능과 안전성을 입증하였으며진행성 간암 치료법을 변화시킬 수 있는 잠재력이 높다"

by Stephen Chan 교수 (홍콩중문대학교)

✓ "위험 대비 치료 이점이 높은 리보세라닙+캄렐리주맙 임상 결과는 사전 전신요법을 받지 않은 비절제성간암 환자들에게 새로운 1차 치료옵션이 될 수 있음을 뒷받침한다"

by Shukui Qin 교수 (중국 난징의과대학교)

Bayer와 Southwestern Texas대학교 논문 (발간일자: 09/12/2023)

P-93 **REAL-WORLD (RW) SYSTEMIC TREATMENT PATTERNS IN US PATIENTS (PTS) WITH HEPATOCELLULAR CARCINOMA (HCC): 2020–2022**

Amit G. Singal [1], Kirhan Özgürdal [2], Xiaozhou Fan [3], Zdravko Vassilev [3], Xiaoyun Pan [3], Chi-Chang Chen [4], Jasjit Multani [5], Zifan Zhou [4], Jing He [6], Federica Pisa [7]

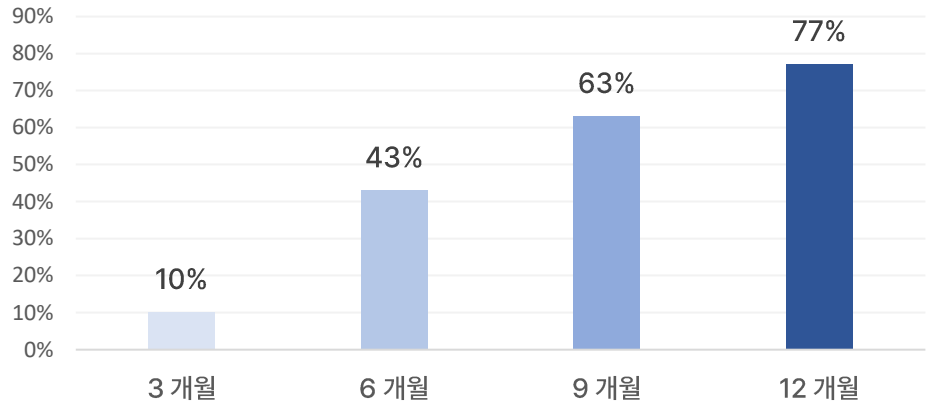
[1] Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA; [2] Bayer Consumer Care AG, Basel, Switzerland; [3] Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA; [4] Real World Evidence Solutions, IQVIA US, Plymouth Meeting, PA, USA; [5] Real World Evidence Solutions, IQVIA US, Falls Church, VA, USA; [6] Advanced Analytics, IQVIA US, Plymouth Meeting, PA, USA, [7] Bayer AG, Berlin, Germany

Introduction: Treatment options for pts with advanced HCC have expanded with the approval of new agents, including atezolizumab plus bevacizumab (atezo+bev), which is the first-line (1L) standard of care for eligible pts. RW evidence for subsequent therapies following atezo+bev is needed as there is no clear guidance on follow-up treatments for HCC. Therefore, this study describes RW treatment patterns in pts who received 1L atezo+bev for HCC in the USA.

Methods: Pts with HCC, aged ≥18 years, who initiated atezo+bev between June 1, 2020, and June 30, 2022, were identified in the IQVIA open-source medical claims and longitudinal prescription databases. Eligible pts had data available for ≥3 months before and ≥2 months after atezo+bev initiation (index date), no prior systemic HCC treatment, and no other prior primary cancers. Pts were followed from the index date until the date of last observation or the end of the study period. Endpoints included the proportion of pts discontinuing atezo+bev, time to atezo+bev discontinuation (TTD), the proportion of pts switching to other systemic treatments, treatment sequence, and time to next treatment (TTNT) in pts with at least 3, 6, 9, or 12 months' follow-up.

Results: Overall, 825 pts were included (median age 67 years [range, 18–85], 80% male) with a median follow-up period of 15.3 months (range, 0.3–28.4). Most pts had compensated liver disease, with a minority having ascites (25%), metastases (22%), esophageal varices (18%), encephalopathy (9%), and gastrointestinal hemorrhage (2%). Portal hypertension was observed in 18% of pts. Esophagogastroduodenoscopy was performed in 18% of pts >1-month post index date. At 3, 6, 9, and 12 months, the proportion of all pts discontinuing atezo+bev was 10%, 43%, 63%, and 77%, the mean TTD (SD) was 21 (0), 63 (31), 92 (53), and 117 (76) days, the proportion of pts switching to other systemic treatments was 4%, 11%, 16%, and 18%, and the mean TTNT (SD) was 62 (21), 104 (41), 138 (65), and 152 (80) days, respectively (Table). Targeted therapies were the most common subsequent therapy (Table); with lenvatinib (6%) and cabozantinib (4%) being the most frequent agents.

Ate/Beva 복용기간 대비 치료 중단율



- ✓ Ate/Beva 복용환자 77%가 12개월 이내 치료를 중단함
- ✓ Ate/Beva의 평균 치료 중단 기간은 5.1개월로 나타남

*대표적인 부작용인 위/장간 출혈로 인한 복용 중단 및 간기능이 악화된 환자에게 약효가 없어 다른 약으로 대체 됐을 거라 판단됨

ESMO 2023 초록 by Eisai (발간일자: 10/23/2023)

1007P - Network meta-analysis (NMA) of lenvatinib vs key comparators in first-line unresectable hepatocellular carcinoma (uHCC)

Presentation Number 1007P
Speakers David Trueman (London, United Kingdom)
Onsite Poster display date Monday, 23 October 2023

Abstract

Background

This research compared the relative efficacy of lenvatinib monotherapy (mono), a standard of care for treatment of uHCC, versus approved / anticipated comparators. Using inverse probability of treatment weighting (IPTW) and an NMA, updated evidence for lenvatinib mono from LEAP-002, in addition to evidence from REFLECT, were included in the analyses.

Methods

Randomized controlled trials (RCTs) were identified via systematic literature review. REFLECT and LEAP-002 investigated lenvatinib mono in uHCC, with patient-level data available for each, however, only REFLECT had a comparator arm of interest. To utilise all available lenvatinib data, the lenvatinib arm from LEAP-002 was adjusted to match aggregate data for confounding factors from REFLECT using IPTW. Weighted Cox regression including matching variables as covariates were used to derive hazard ratios (HRs) for OS and progression-free survival (PFS) comparing lenvatinib and sorafenib. The estimated HRs were included in fixed-effects Bayesian NMAs to compare lenvatinib and comparators. Scenario analyses explored alternative choices for IPTW estimators.

Results

Eight RCTs (including REFLECT) and adjusted data from LEAP-002, were included in the NMA. Lenvatinib demonstrated a significant improvement in OS compared with sorafenib, and significant improvement in PFS compared with sorafenib, tremelimumab + durvalumab, tislelizumab and durvalumab (Table).

Results

Eight RCTs (including REFLECT) and adjusted data from LEAP-002, were included in the NMA. Lenvatinib demonstrated a significant improvement in OS compared with sorafenib, and significant improvement in PFS compared with sorafenib, tremelimumab + durvalumab, tislelizumab and durvalumab (Table).

Table: 1007P

NMA results for OS and PFS – lenvatinib vs comparator

Comparator	OS; median HR (95% CrI)	PFS; median HR (95% CrI)
Sorafenib	0.75 (0.66, 0.86)	0.57 (0.49, 0.66)
Durvalumab	0.88 (0.71, 1.08)	0.55 (0.45, 0.69)
Tislelizumab	0.88 (0.71, 1.11)	0.51 (0.41, 0.65)
Tremelimumab 300 mg + durvalumab	0.97 (0.77, 1.20)	0.63 (0.51, 0.78)
Atezolizumab + bevacizumab	1.14 (0.86, 1.51)	0.87 (0.67, 1.13)
Camrelizumab + apatinib	1.21 (0.92, 1.60)	1.09 (0.82, 1.44)

Bold = significant resultAbbreviations: CrI, credible interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival

Conclusions

These results suggest that patients with uHCC treated with lenvatinib mono have similar or significantly improved OS and PFS when compared with other therapies.

Legal entity responsible for the study

Eisai Inc.

Funding

Eisai Inc.

- ✓ 경쟁사인 Eisai가 ESMO 2023에서 발표한 OS/PFS HR에 관해 논문 발표
- ✓ 시판중인 4개 약물 및 시판 예상되는 약물 (리보세라닙/캄렐리주맙)의 Lenvatinib 대비 효능 비교 분석

*주요 간암 1차 치료제 대비 HLB의 리보세라닙/캄렐리주맙이 OS/PFS HR Best in Class로 검증됨

감사합니다

HLB 글로벌투자전략팀