HLB

Human Life Better

July 2024

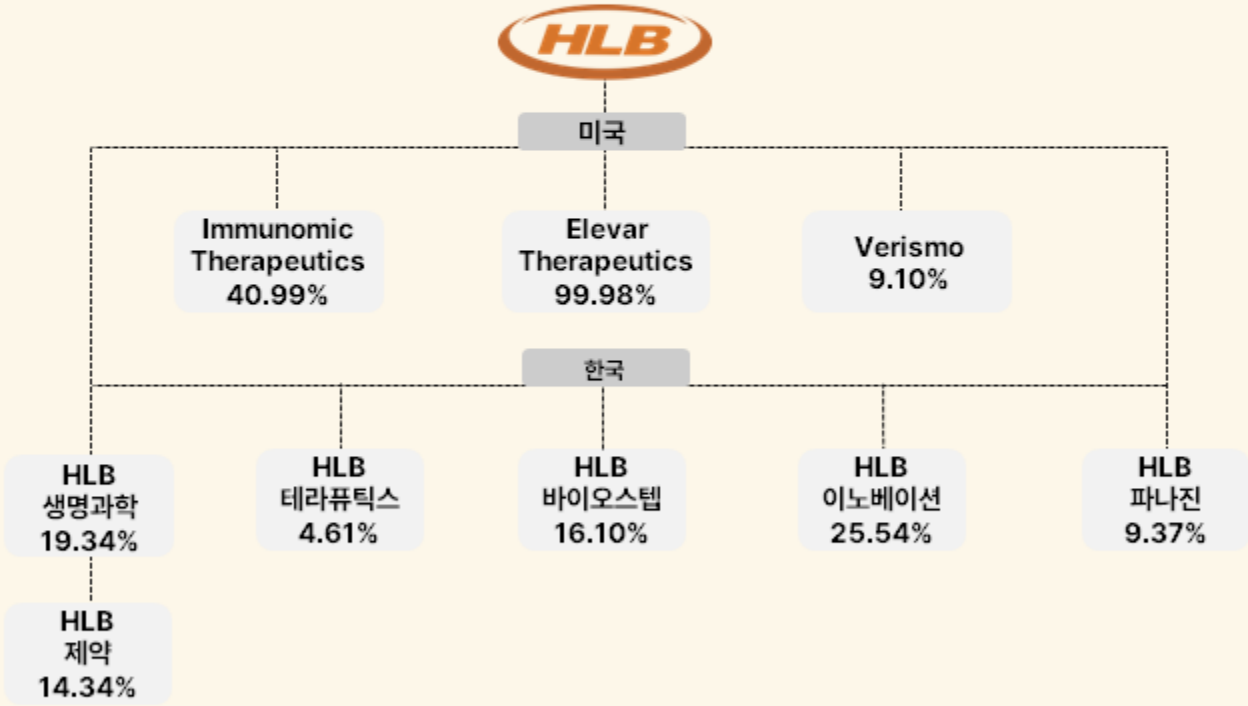
회사 개요

회사 요약

대표이사	진양곤, 백윤기
R&D 인력	182명
사업	Bio, Healthcare
자본 총계(2024. 03)	6,509억원
자산 총계 (2024. 03)	8,616억원
부채 총계 (2024. 03)	2,107억원
부채 비율 (2024. 03)	24.5%
시가총액 (2024.07.22)	10조 7,945억원

연결재무제표 기준

HLB 계열사 구조



출처: 2024 1분기 보고서

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	
HLB Therapeutics	안구건조증	글로벌	RGN-259 단독	
	신경 영양성 각막염			

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

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	***23.8 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	****CRL Issued**	2020년 승인	2022년 승인	2018년 승인	2007년 승인

출처: Clinical Trail Gov.
*ASCO2024에서 22.1개월에서 23.8개월로 임상데이터 업데이트 됨, **CRL (Complete Response Letter)= 승인 보류 및 서류보완

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 **완료**

2024. 05
- 5/16/24, **CRL Issued**

CRL 이슈 이후 진행상황

2023. 12
- CMC관련 10가지 질문지 수령

2024. 2/3
- CMC관련 답변서 제출 (2번)

2024. 5.16
- CRL 수령

2024. 7. 02
- PAL 수령, 추가지적 사항 없음
- TYPE A 미팅 성공적으로 마무리
- FDA에서 재신청 요청

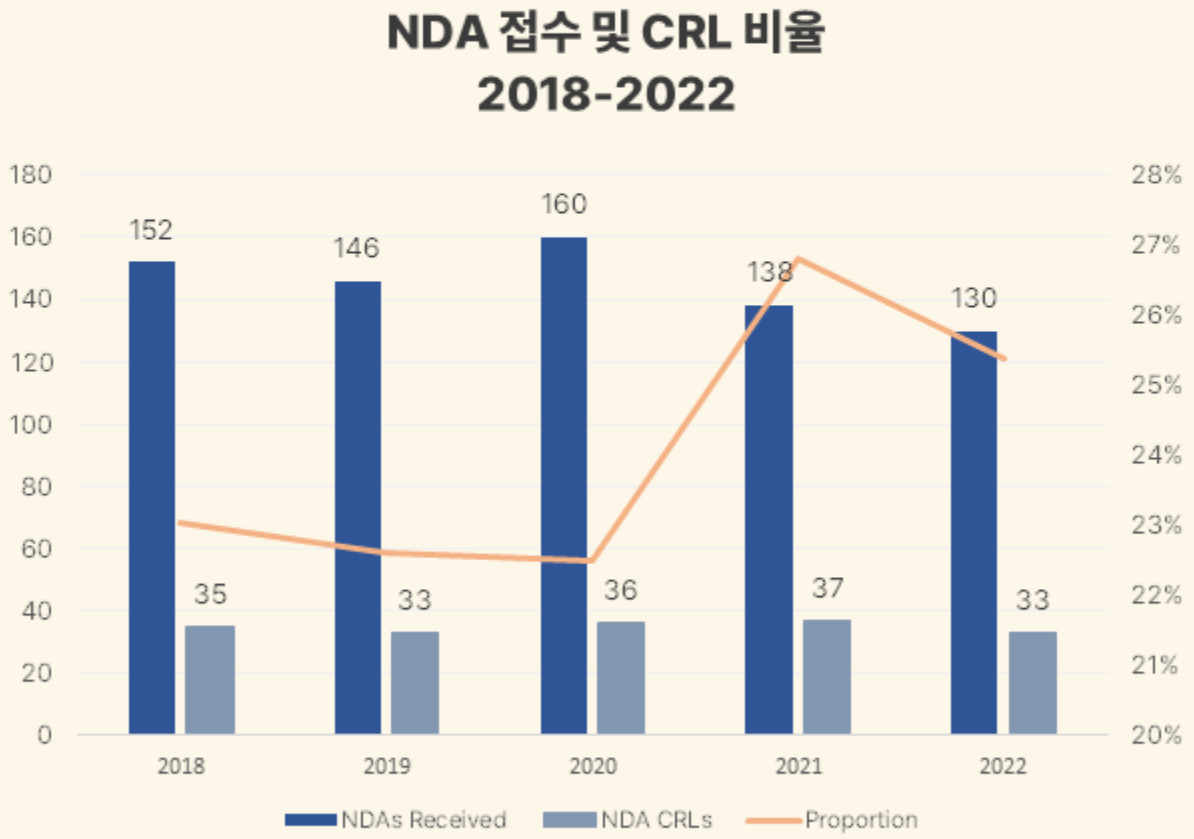
2024. 9
- NDA 재신청 계획
- 23.8개월 OS데이터 업데이트 자료 제출 예정

2025. 3
CLASS 2일 경우 결과 발표 시점

OR

2024. 11
CLASS 1일 경우 결과 발표 시점

CRL Trends



24%

과거 5개년도 NDA 신청 접수 중 CRL 받은 평균 비율

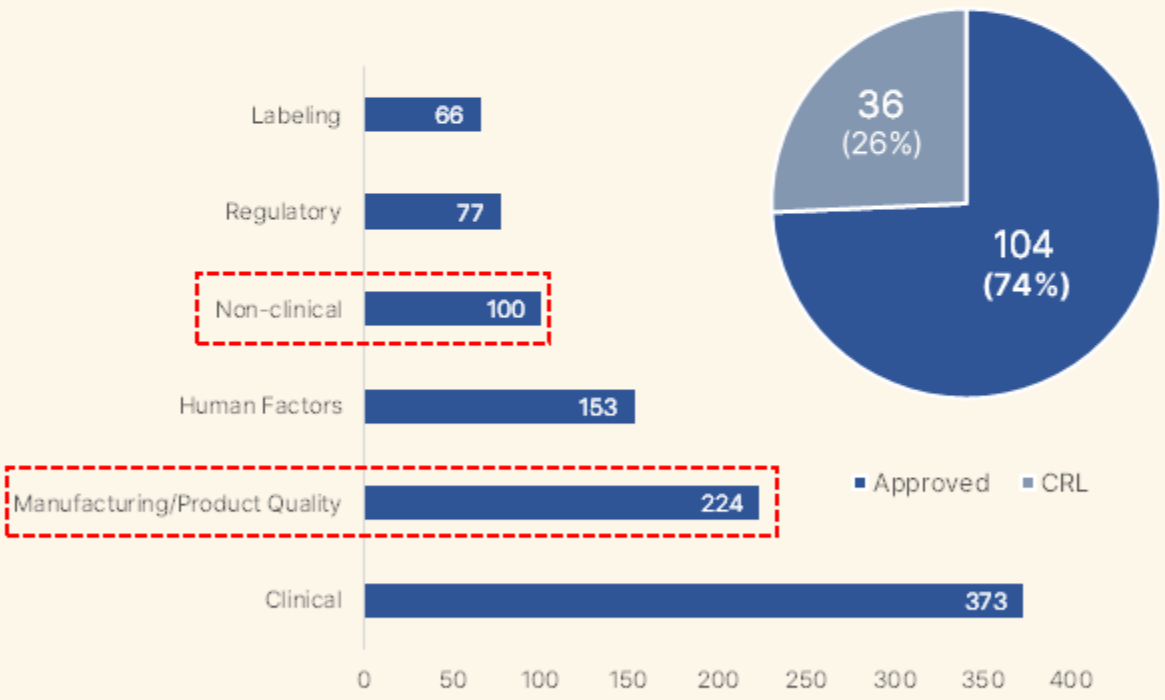
89%

CMC관련으로 CRL 건수의 승인율로 CRL 이슈 중 가장 높음
(임상 결함에 의한 CRL의 경우 24%만 승인)

출처: WELLS FARGO Research, FDA CRL Deep Dive, June 6, 2024

CRL Trends

CRL TYPE별 재신청 소요기간 및 CRL이후 승인율



100~224일

당사 예상 재신청 소요 기간
(Nonclinical or Manufacturing)

74%

CRL 이후 NDA 승인율
(26%는 불허가 아닌 또 다른 CRL이슈)

출처: WELLS FARGO Research, FDA CRL Deep Dive, June 6, 2024

간암1차치료제 경쟁사 Updated Data 비교분석

간암1차치료제 기존데이터 대비 옵디보/여보이 대조군 기준 Spread 분석

단위: 개월 수

약물명	실험군	대조군	실험군-대조군 차이	
	mOS		Spread	*Adj. Spread
Rivo.+Cam.	23.8	15.2	8.6	**7.56**
Ate.+Bev.	19.2	13.4	5.8	4.76
Trem.+Dur.	16.4	13.8	2.6	1.56
Lenvatinib	13.6	12.3	1.3	
Nivo.+Ipl.	23.7	20.9	**2.8**	

*Adj. Spread는 옵디보/여보이 임상 대조군 Lenvatinib/Sorafenib 8:2 비율의 임상군을 적용하여 Lenvatinib (13.6-12.3)x0.8=1.04를 다른 경쟁사에게 적용시켜 계산함.

- ✓ 6/04/24기준, 옵디보/여보이 병용 간암1차치료제 임상3상 중간결과 데이터 발표.
- ✓ mOS 23.7개월로 당사 23.8개월과 차이가 크진 않지만, 옵디보/여보이 대조군 기준 **4.76개월** 리보세라닙/캄렐리주맙 생존기간이 더 높음.

출처: 각 사 공식홈페이지 IR섹션

간암1차치료제 경쟁사 Updated Data 비교분석

Rivoceranib+Camrelizumab vs. Nivolumab+Ipilimumab

임상지표	실험군	대조군	실험군	대조군	비고
	Rivo+Cam	Sorafenib	Nivo+Ipl	LEN/SOR	
mOS	23.8	15.2	23.7	20.6	
ORR	25.4	5.9	36	13	331% vs. 177%
TRAE	24.3%		41%		
HR (95% CI); p valule	0.64		0.79		FDA 승인 기준 0.8

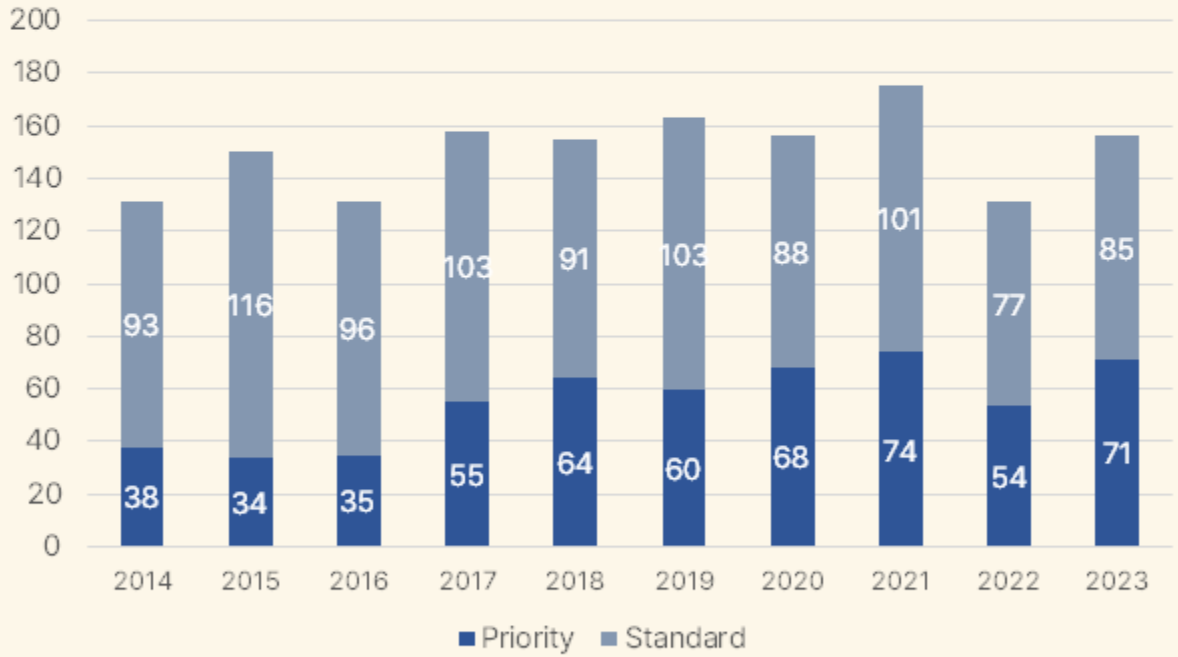
✓ 객관적반응률(ORR)에서 리보세라닙/캄렐리주맙 병용치료제는 331%로 BMS제품 대비 약 1.87배 가량 높게 나타남.

- BMS의 제품은 면역항암제+면역항암제 병용요법으로 specific한 환자에게만 약효가 높은 한계점을 보임.

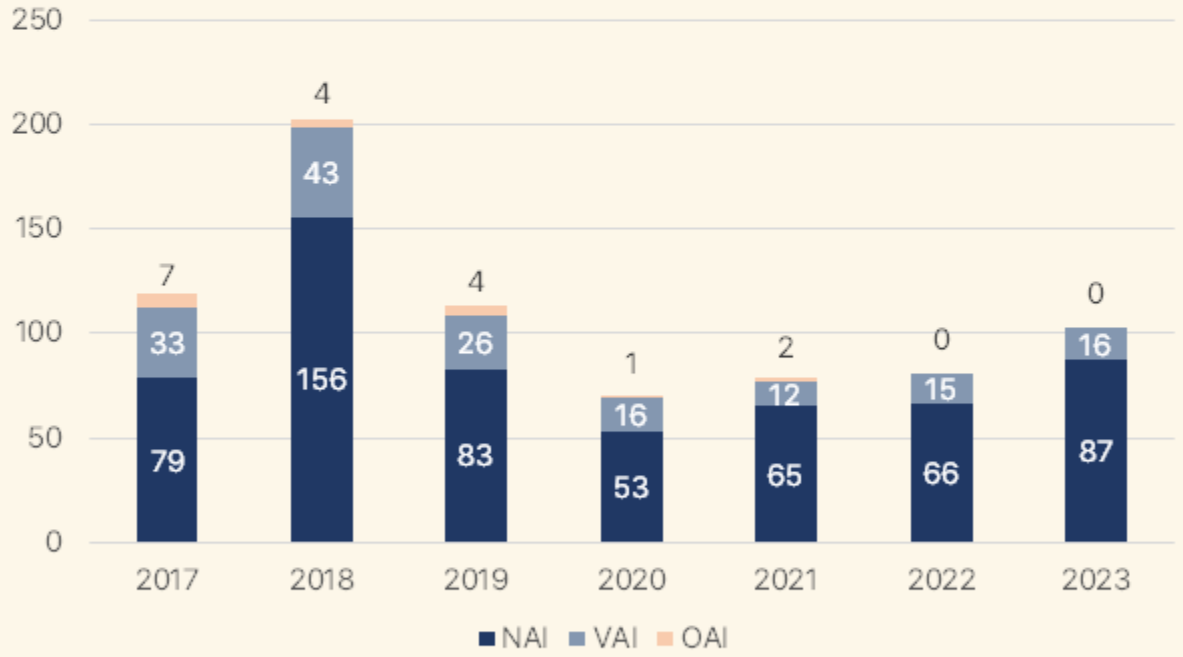
✓ TRAE (Grade 3이상)지표에서 BMS 제품은 약 41%로 당사의 제품보다 부작용이 높은 걸로 나타남.

PUDFA Trend Graphs

FDA NDA 신청 건 수



BIMO Inspection

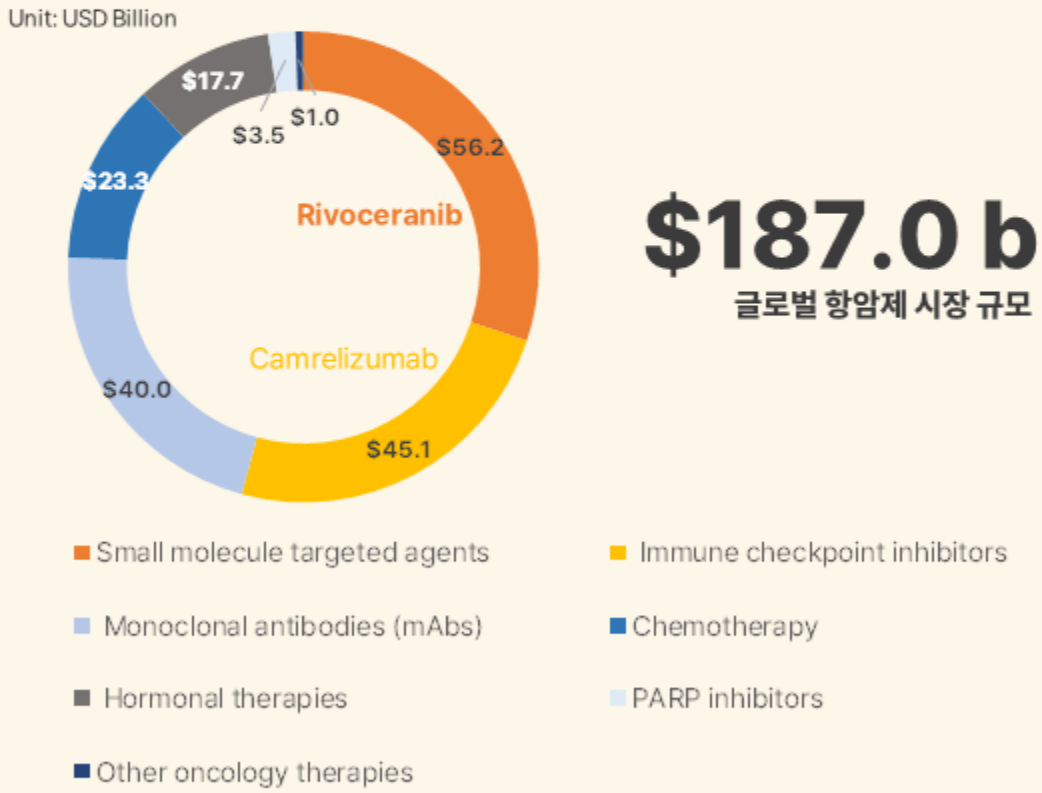


글로벌 간암 환자 수

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

글로벌 항암제 시장 가치

글로벌 항암제 분야별 시장 규모



$187.0 bn

글로벌 항암제 시장 규모

Unmet Need 수요 및 글로벌 시장

2nd

글로벌 주요 사망 원인 2위 (암)

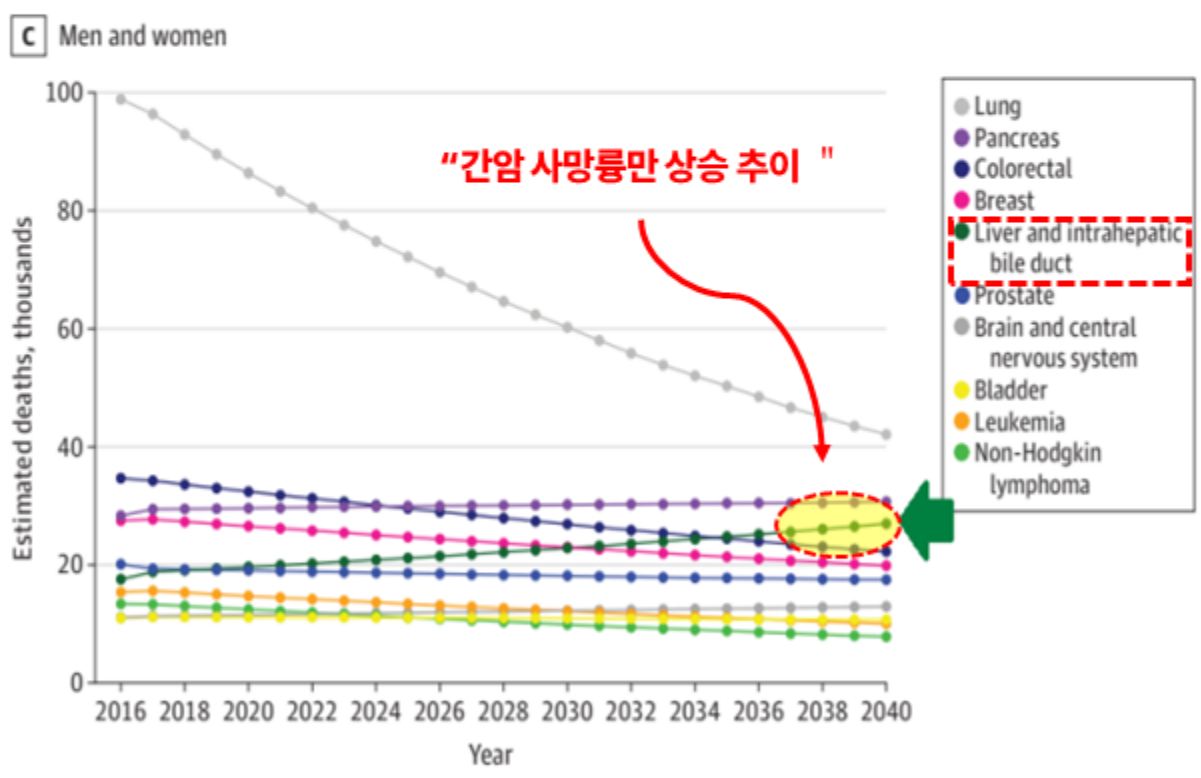
16.3m

2040년까지 암은 매년 1,630만명의 사망 원인이 될 것임

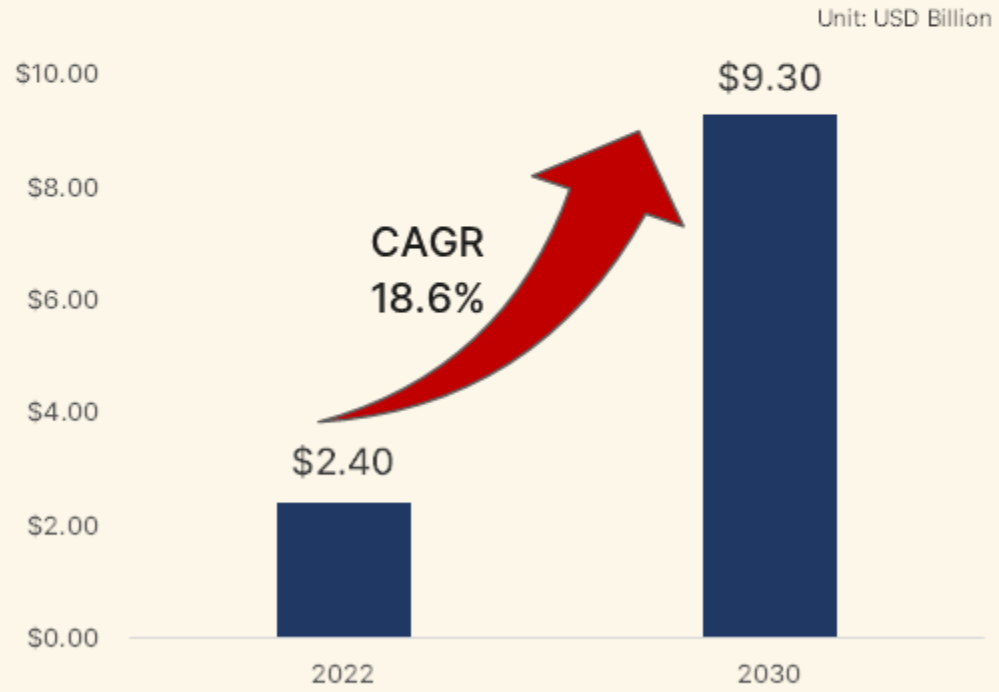
출처: IQVIA

간암1차치료제 시장 성장성

글로벌 암 환자 사망률 추이

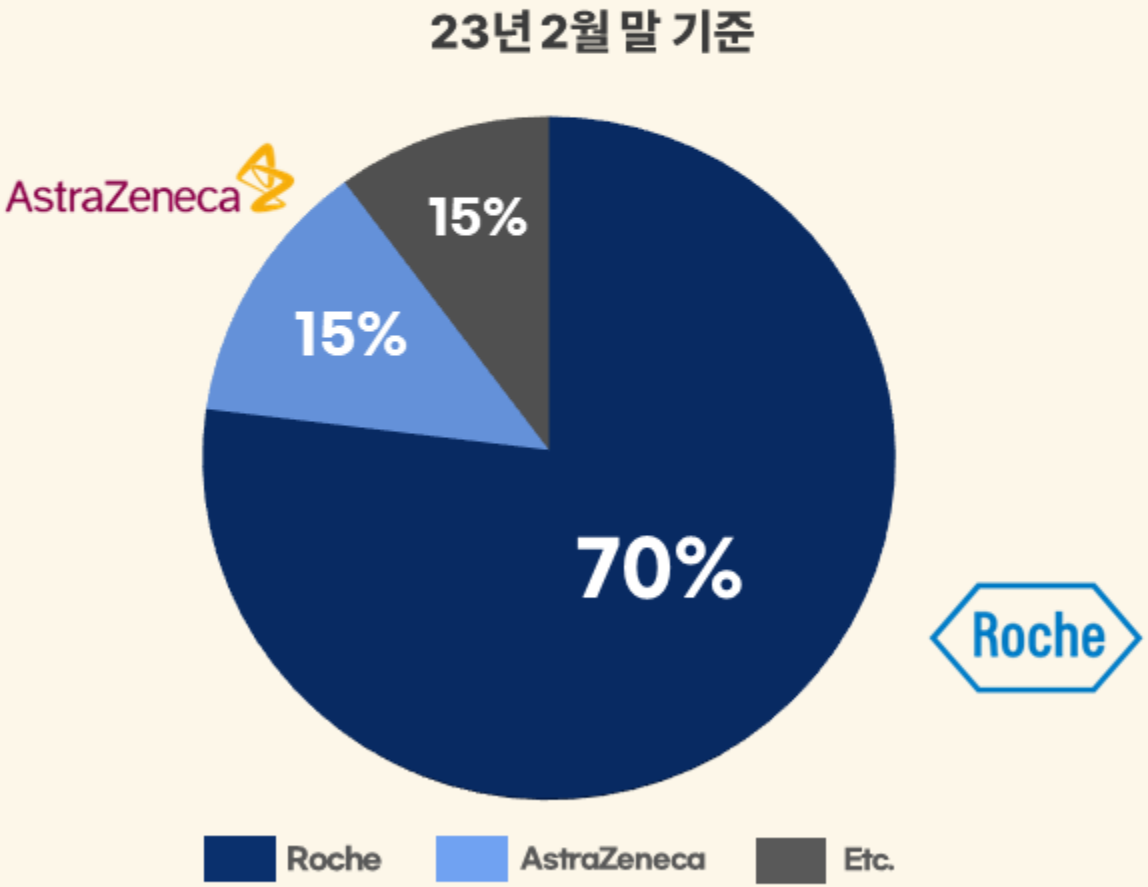


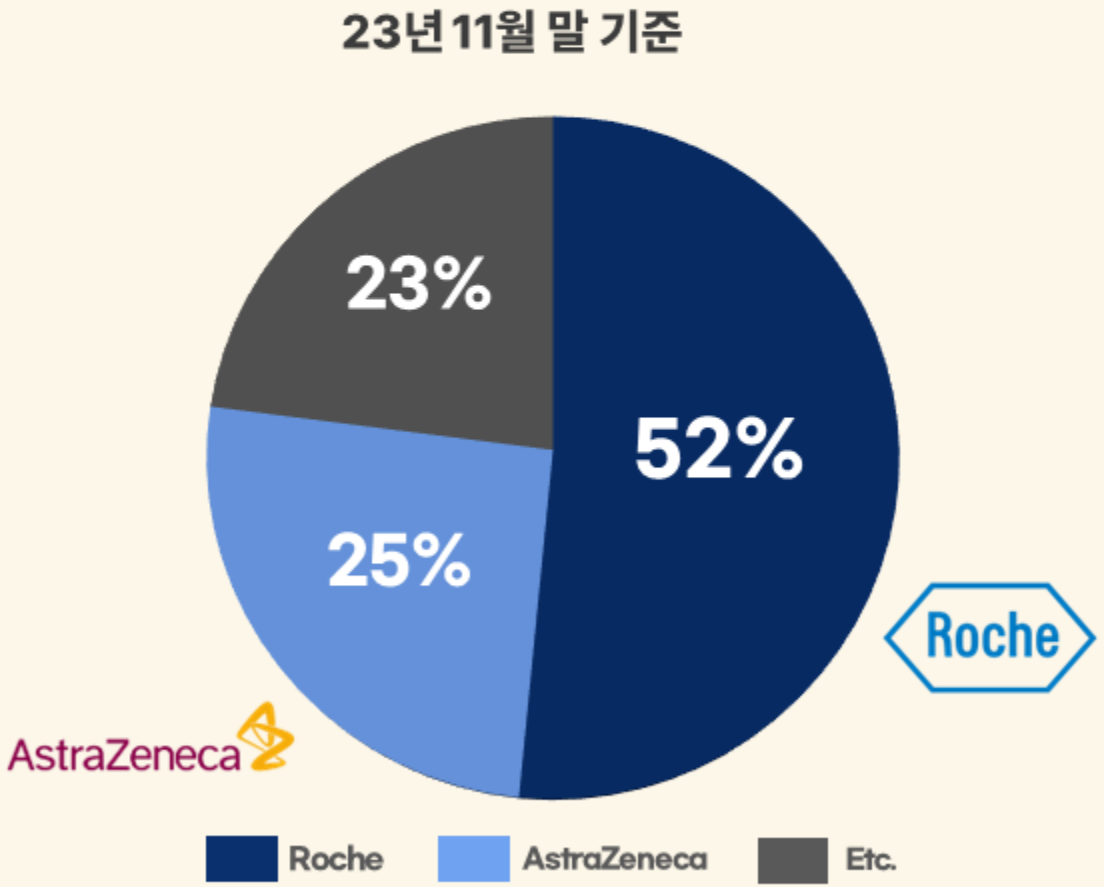
글로벌 간암 치료제 시장 규모



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

간암1차 시장 경쟁사 점유율





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

간암1차 치료제 NDA승인이후 매출 추이

Unit: USD Million

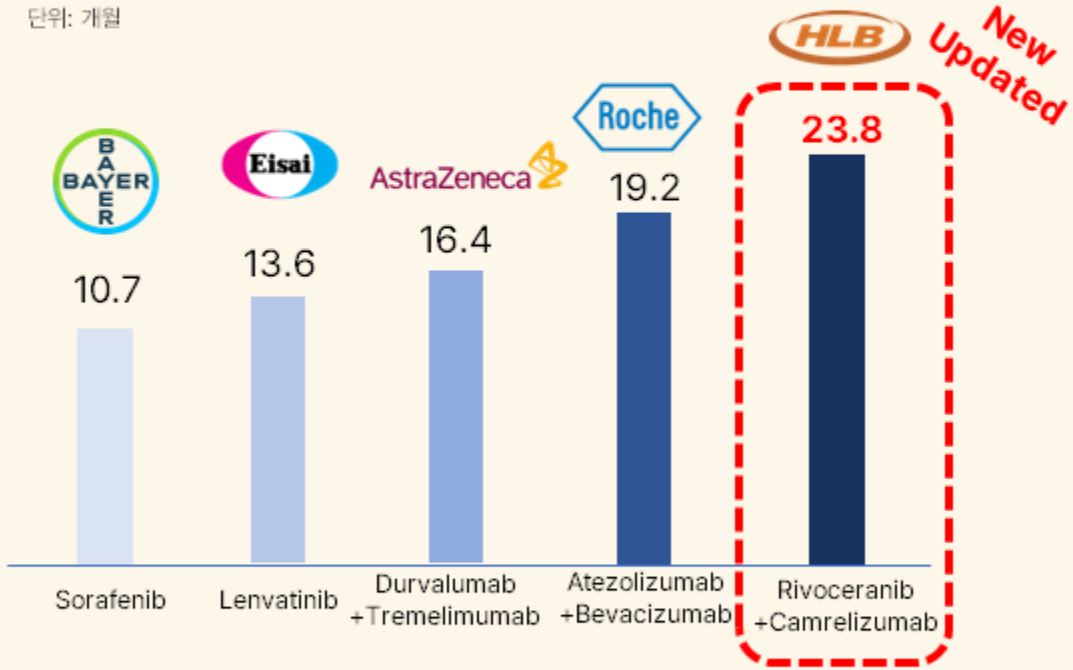
회사	약물	매출					
		2018	2019	2020	2021	2022	2023
Roche	Avastin			5,319	3,343	2,321	1,757
	Tecentriq			2,919	4,326	3,894	4,206
AstraZeneca	Imfinzi					*2,784	*4,237
	Imjudo						
Eisai	Lenvima	390	697.2	834.3	1,198	1,555	1,854
		2009	2010	2011	2012		
Bayer	Sorafenib	117.69	115.53	151.78	217.5		

*AstraZeneca 2022,2023년 Annual Report에 Imfinzi 매출에 Imjudo매출이 포함되어 있다 명시됨.

출처: Bloomberg, 각 사 Annual Report

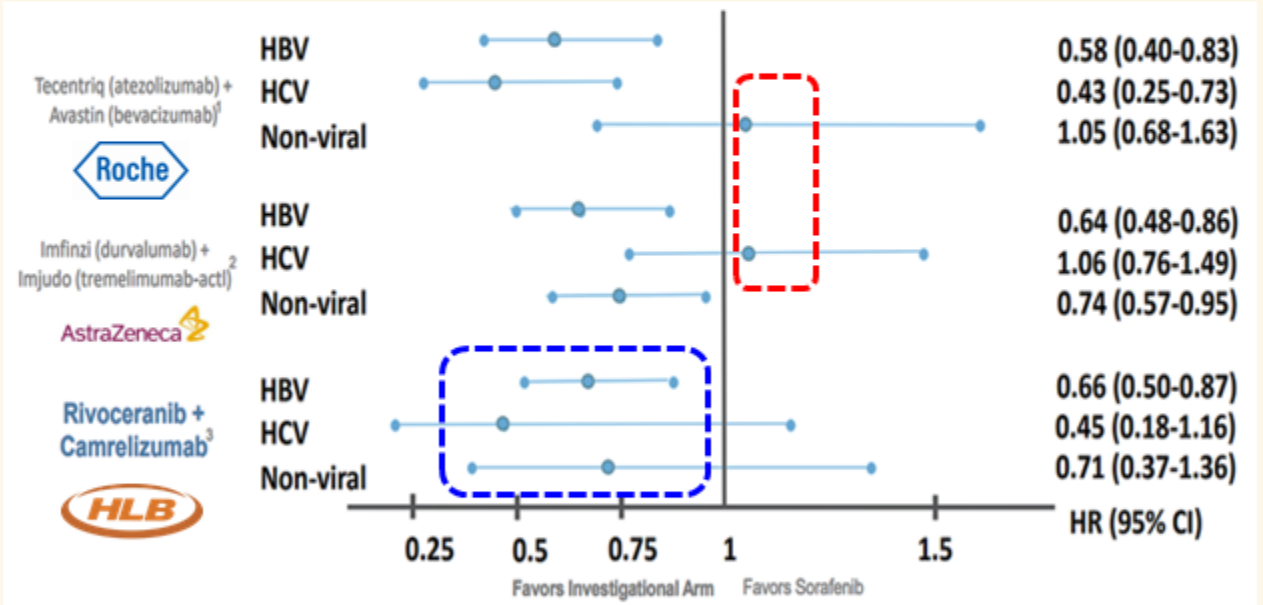
Best-in-Class 임상데이터

간암 1차치료제 OS (생존 기간) 비교



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

간암 발병 인자 종류별 약효 비교



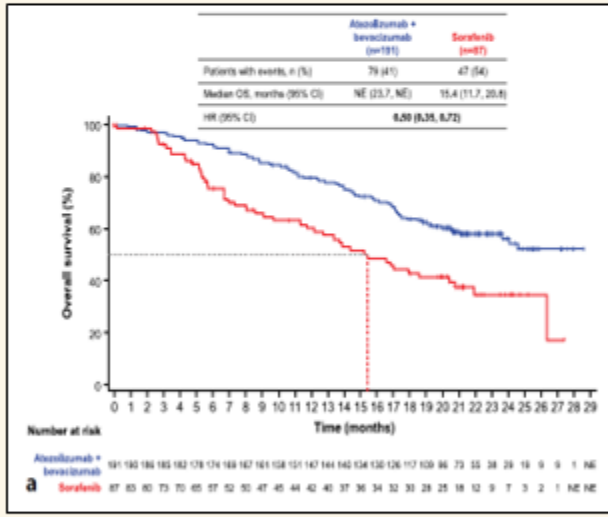
✓ 현 간암1차치료제 중 리보세라닙/캄렐리주맙이 유일하게 모든 발병원인 환자군에게 높은 약효가 입증됨

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

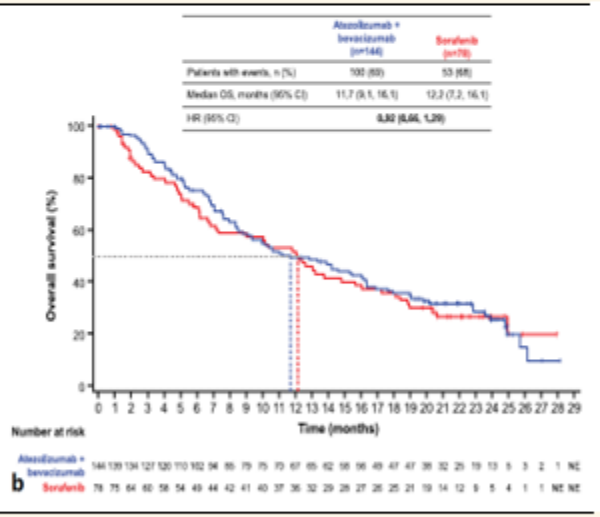
Best-in-Class 임상데이터

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

ALBI 1 Grade



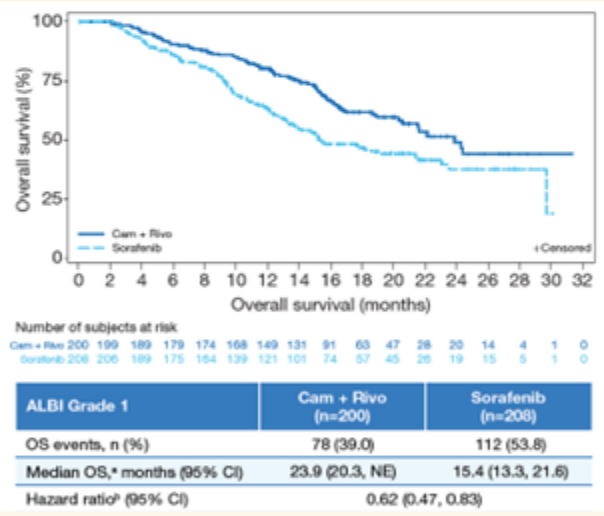
ALBI 2 Grade



- ✓ 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)

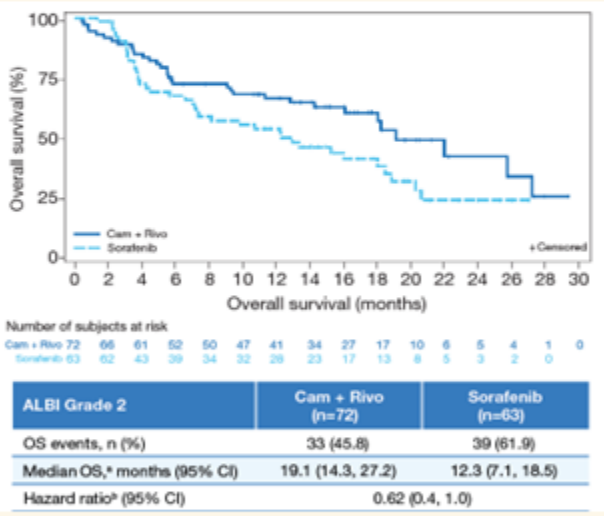
CARES-310 (HLB & Elevar)
Rivoceranib + Camrelizumab

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 ratioᵇ (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 ratioᵇ (95% CI)	0.62 (0.4, 1.0)	

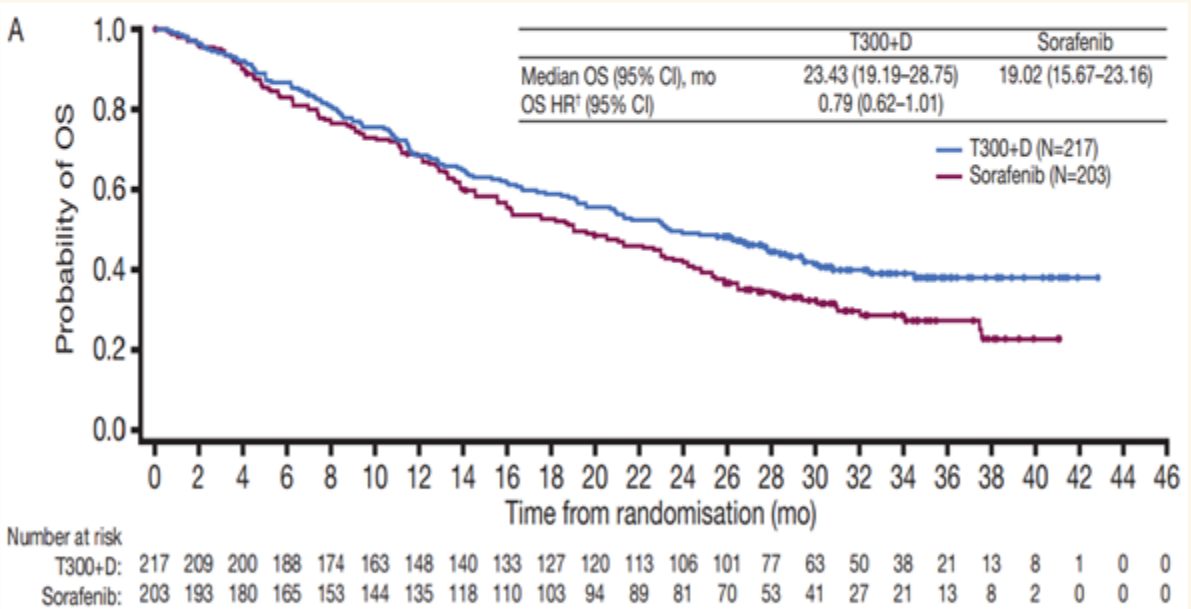
- ✓ ALBI 등급에 상관없이 모든 환자군에 약효가 좋으며 특히 Ate/Beva에서 약효가 없는 ALBI 2등급 환자들에게 우월한 약효를 나타냄
- ✓ ALBI G1 HR: 0.62 (0.47-0.83), ALBI G2 HR: 0.62 (0.4-1.0)

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

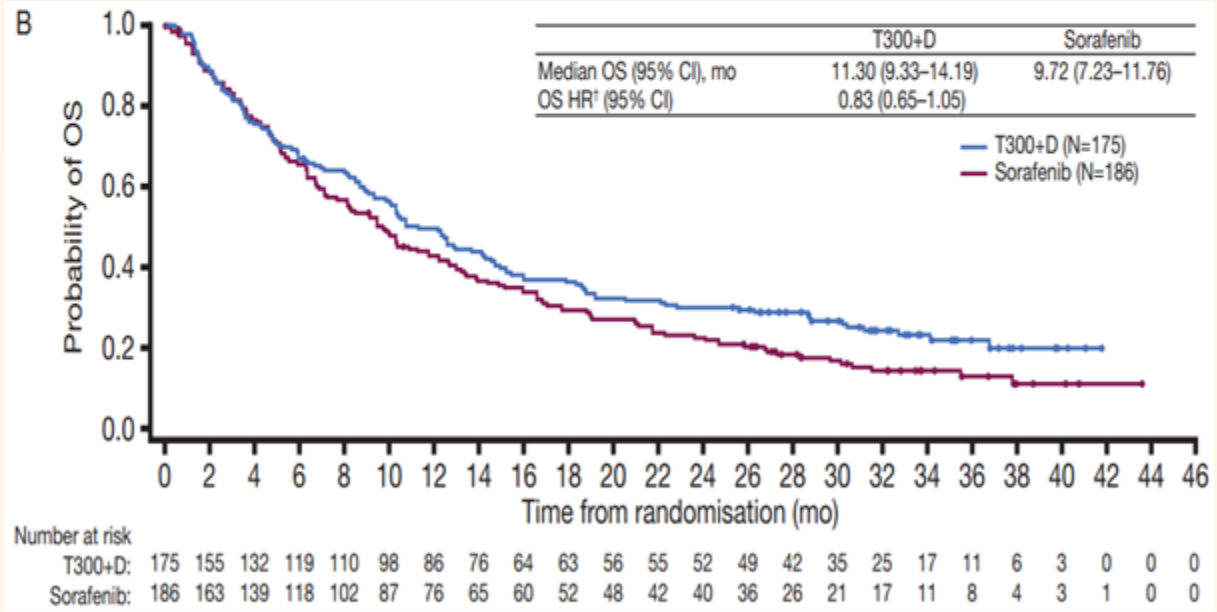
Best-in-Class 임상데이터

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

ALBI Grade 1



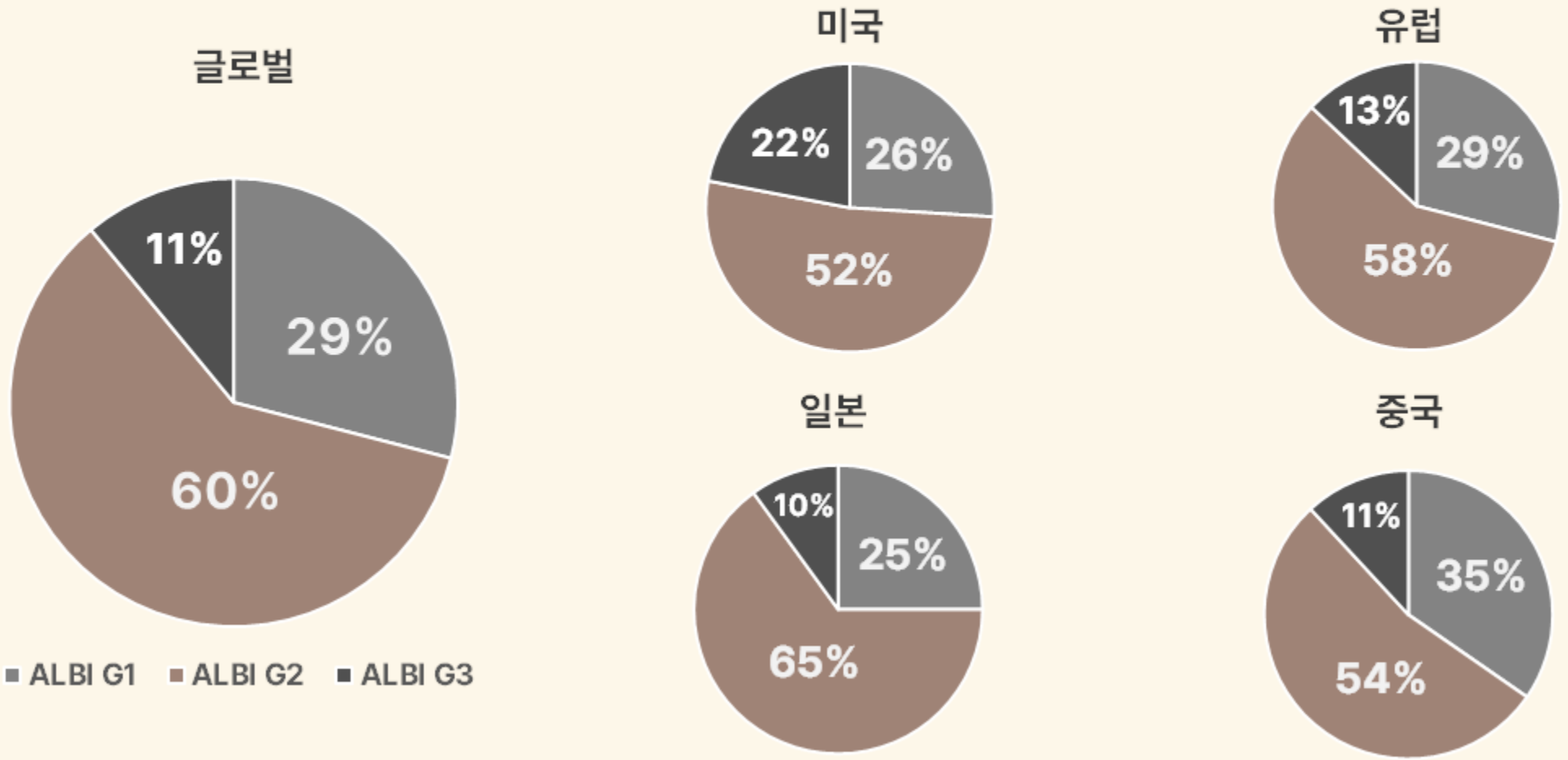
ALBI Grade



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

출처: Abou-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

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+Ipilimumab	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 내** 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

글로벌논문데이터

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)

글로벌논문데이터

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]

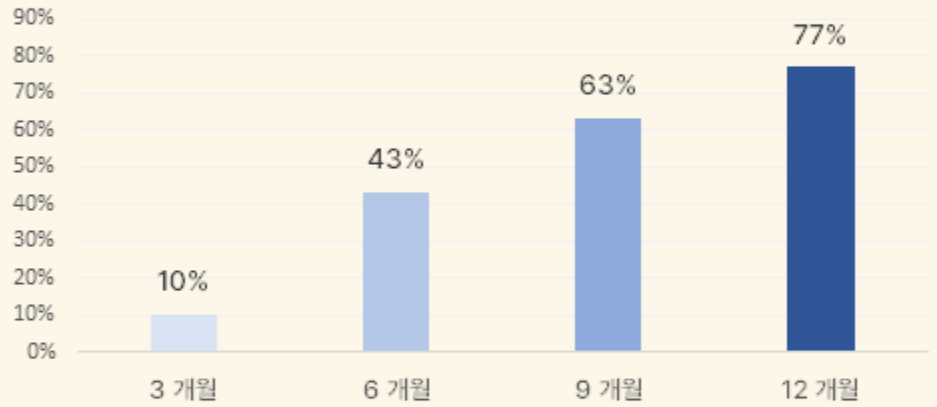
[1] Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA; [2] Bayer Consumer Care AG, Basel, Switzerland; [3] Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA; [4] Real World Evidence Solutions, IQVIA US, Plymouth Meeting, PA, USA; [5] Real World Evidence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

글로벌논문데이터

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

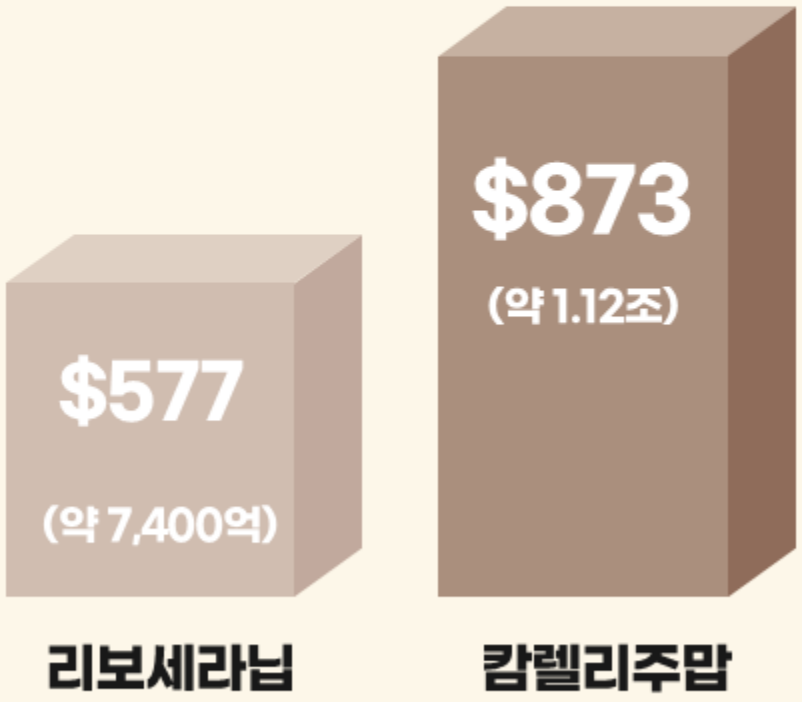
Eisai Inc.

- ✓ 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

리보세라닙 적응증 확장성

리보세라닙/캄렐리주맙 중국 내 매출 (2023)



감사합니다.

HLB

Human Life Better