Phase 3 ClarIDHy Update at ESMO

September 30, 2019

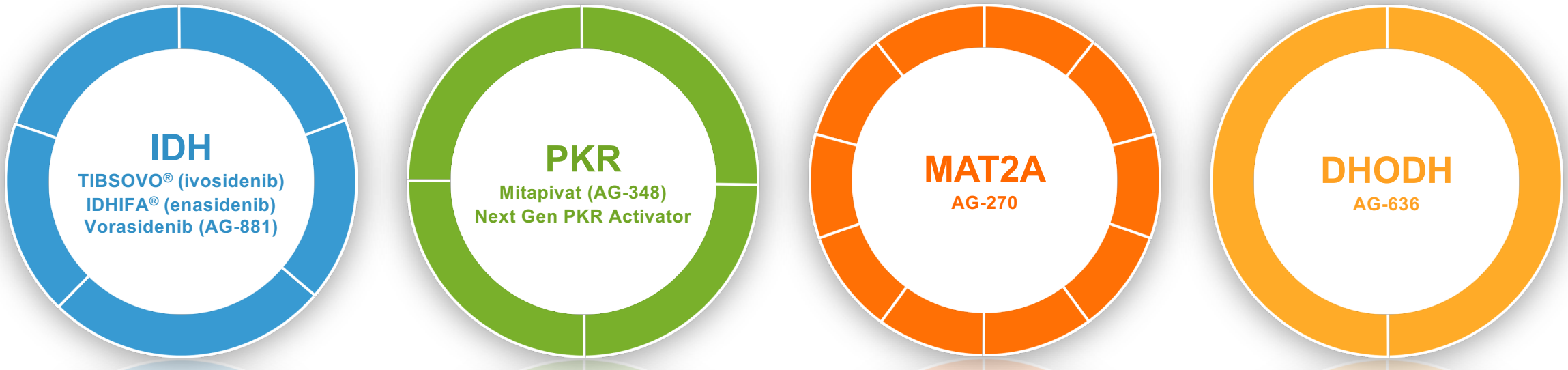
Today's Agenda

- Opening Remarks – **Jackie Fouse, Ph.D.,** Chief Executive Officer
- Overview of Cholangiocarcinoma – **Susan Pandya, M.D.,** Vice President, Clinical Development
- ClarIDHy Trial Results – **Andrew X. Zhu, M.D., Ph.D.,** Professor of Medicine at Harvard Medical School and Attending Oncologist at Massachusetts General Hospital
- Q&A – **Andrew Zhu, Jackie Fouse, Chris Bowden & Susan Pandya**

Forward Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Agios' plans, strategies and expectations for its and its collaborator's preclinical, clinical and commercial advancement of its drug development programs including TIBSOVO® (ivosidenib); the potential benefits of Agios' product candidates; its key milestones for 2019; its plans regarding future data presentations; and the potential benefit of its strategic plans and focus. The words "anticipate," "expect," "hope," "milestone," "plan," "potential," "possible," "strategy," "will," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios' current expectations and beliefs. For example, there can be no guarantee that any product candidate Agios or its collaborators is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios' product candidates will successfully continue. There can be no guarantee that any positive developments in Agios' business will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this presentation and various remarks we make during this presentation could also be affected by risks and uncertainties relating to a number of other important factors, including: Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to maintain key collaborations; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this presentation and various remarks we make during this presentation speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



AML
Low Grade Glioma
Cholangiocarcinoma
Chondrosarcoma
MDS

Adult PK Deficiency
Pediatric PK Deficiency
Sickle Cell Disease
Thalassemia

NSCLC
Bladder
Melanoma
Head & Neck
Pancreatic

Glioblastoma
DLBCL
Esophageal
Gastric
Mesothelioma

Lymphoma
AML

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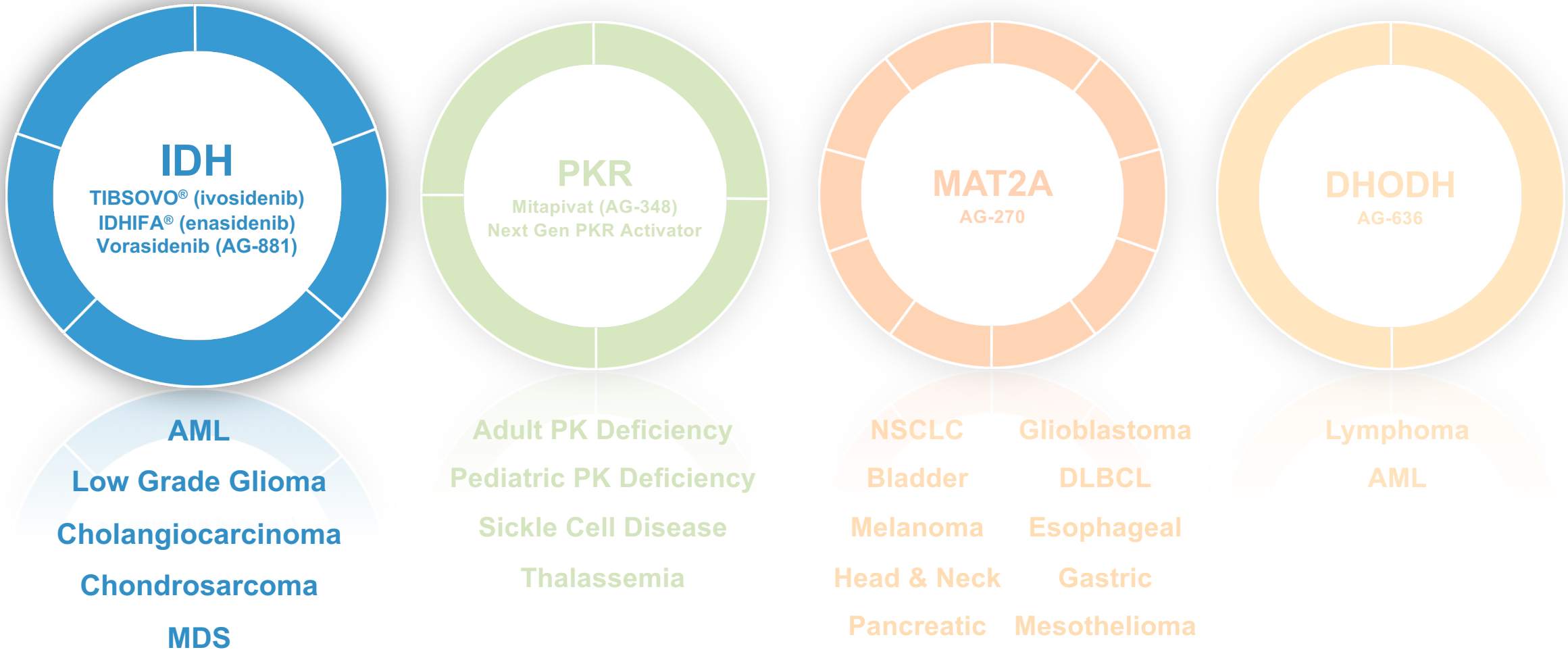
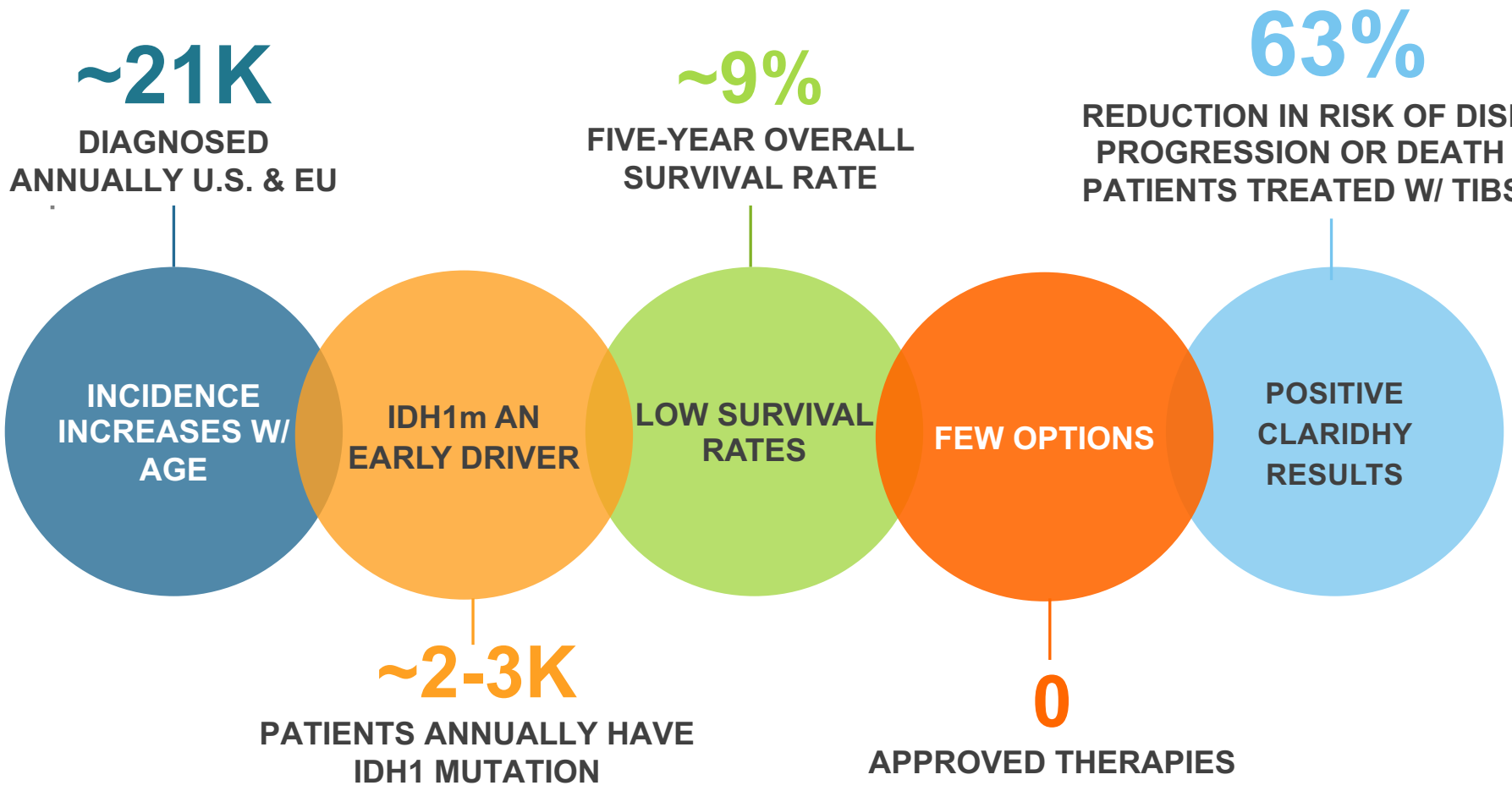


Opportunity for an IDH1m Inhibitor in Solid Tumors

- Frequency of IDH1 mutation in a variety of solid tumors + unmet need in these indications = opportunity to make a difference in the treatment paradigm for these patients
- Active clinical development in cholangiocarcinoma & glioma
- Understanding the IDH mutation's role in the treatment of solid tumors is evolving

Plan to File sNDA for TIBSOVO® in Second-line or Later Cholangiocarcinoma by Year-end 2019

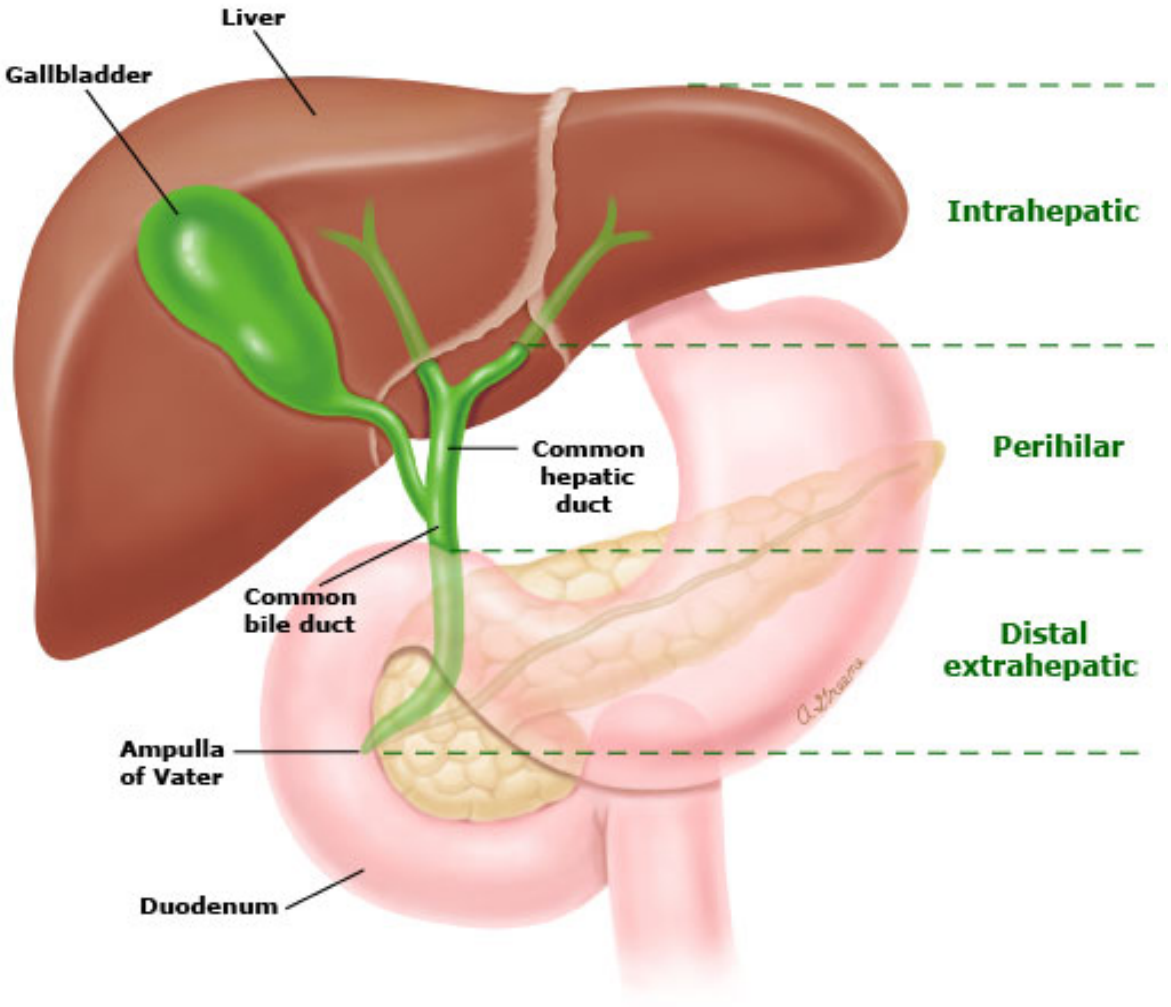


Sources: CDC National Program of Cancer Registries (NPCR); Epiphany Partners Epic Oncology; Decision Resources; Market Research; Borger DR et al. Oncologist 2012;17:72-9.; Kipp BR et al. Hum Pathol 2012;43:1552-8.; Goyal L et al. Oncologist 2015;20:1019-27; data from ASCO 2017

Cholangiocarcinoma Overview

Susan Pandya, M.D., Vice President, Clinical Development

Cholangiocarcinoma a Devastating Disease with No Approved Targeted Therapies



Symptoms:

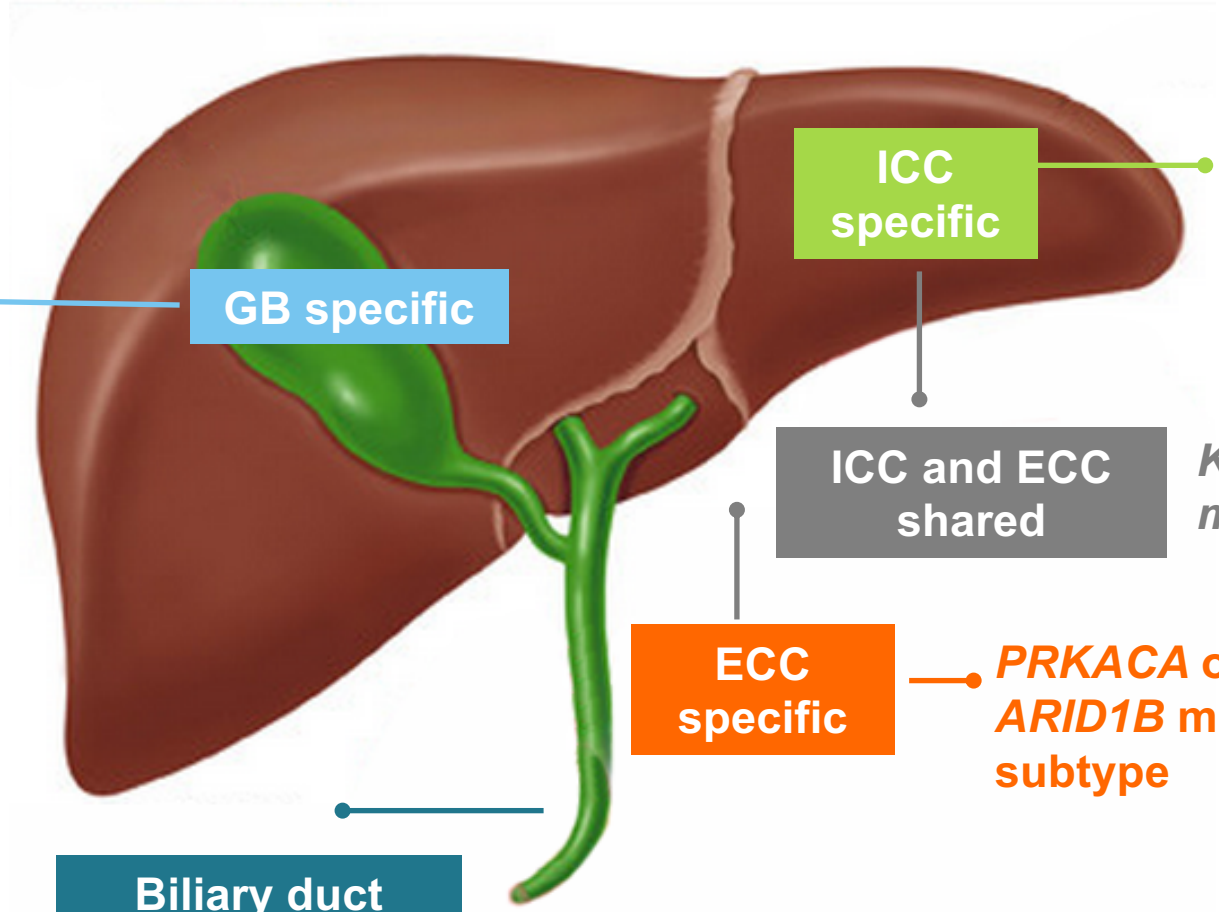
- Abdominal pain (30-50%)
- Weight loss (30-50%)
- Fever (20%)
- Itching
- Jaundice

Increase in laboratory tests:

- Alkaline phosphatase
- GGT
- Total (direct) bilirubin
- AST/ALT
- CA 19-9 (elevated in ~65% cholangiocarcinoma)

Sources: http://www.alltohealth.com; www.uptodate.com; https://gi.jhsps.org

Genetic Alterations in Biliary Tract Cancer



***EGFR, ERBB3, PTEN, ARID2, MLL2, MLL3, TERT* promoter mutation APOBEC signature**

IDH1/2, FGFR2 fusion, EPHA2, BAP1 mutation

C>T at CpG signature

KRAS, SMAD4, ARID1A, GNAS mutation

***PRKACA* or *PRKACB* fusion, *ELF3*, *ARID1B* mutation, better prognosis subtype**

TP53, BRCA1, BRCA2, PIK3CA mutation

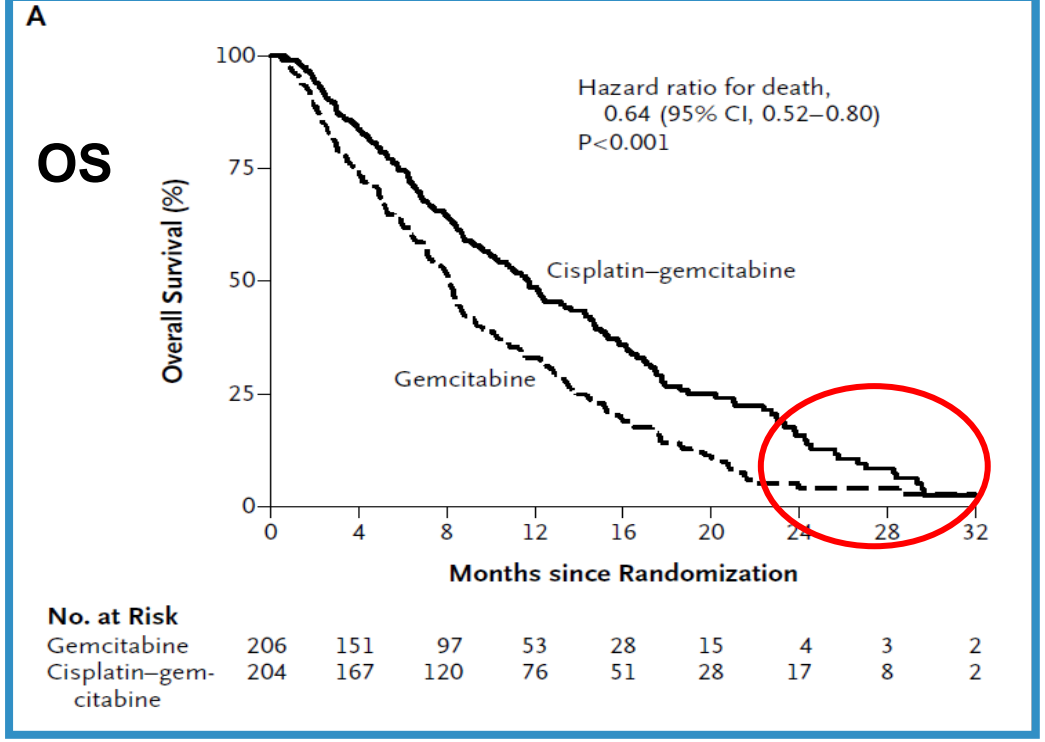
Poor-prognosis subtype with high immune checkpoint activity

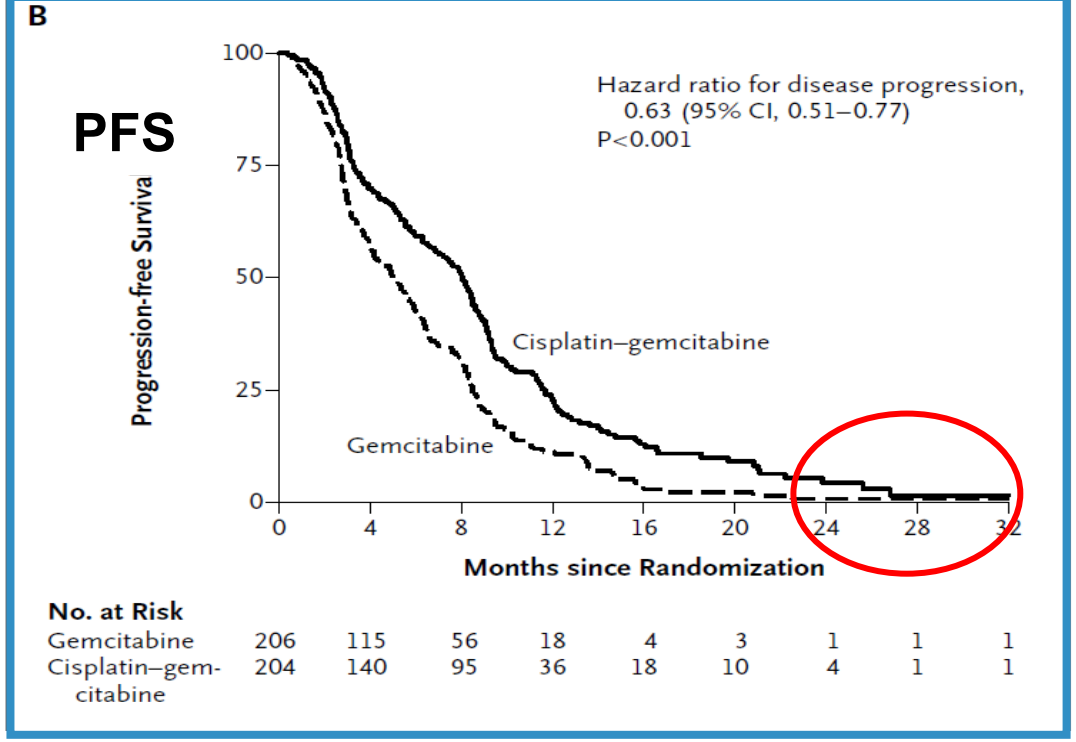
Source: © Nakamura et al, Nature Genetics 2015

Current Treatments are Limited to Chemotherapy-Based Regimens

Phase 3 ABC-02 Gemcitabine and Cisplatin – standard of care for newly diagnosed metastatic disease

- OS – 11.7 months Gem/Cis vs. 8 months for Gem alone
- PFS – 8 months for Gem/Cis vs. 5 months for Gem alone



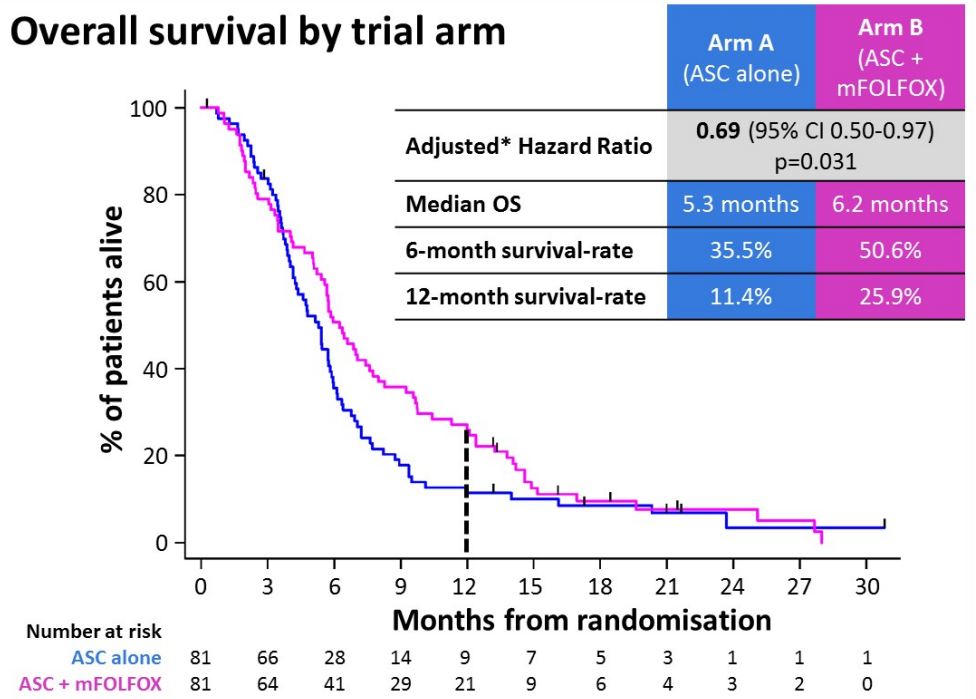


Source: Valle J. N Engl J Med. 2010

Outcomes with Second Line Chemotherapy Remain Poor and Highlight Need for Novel Treatments

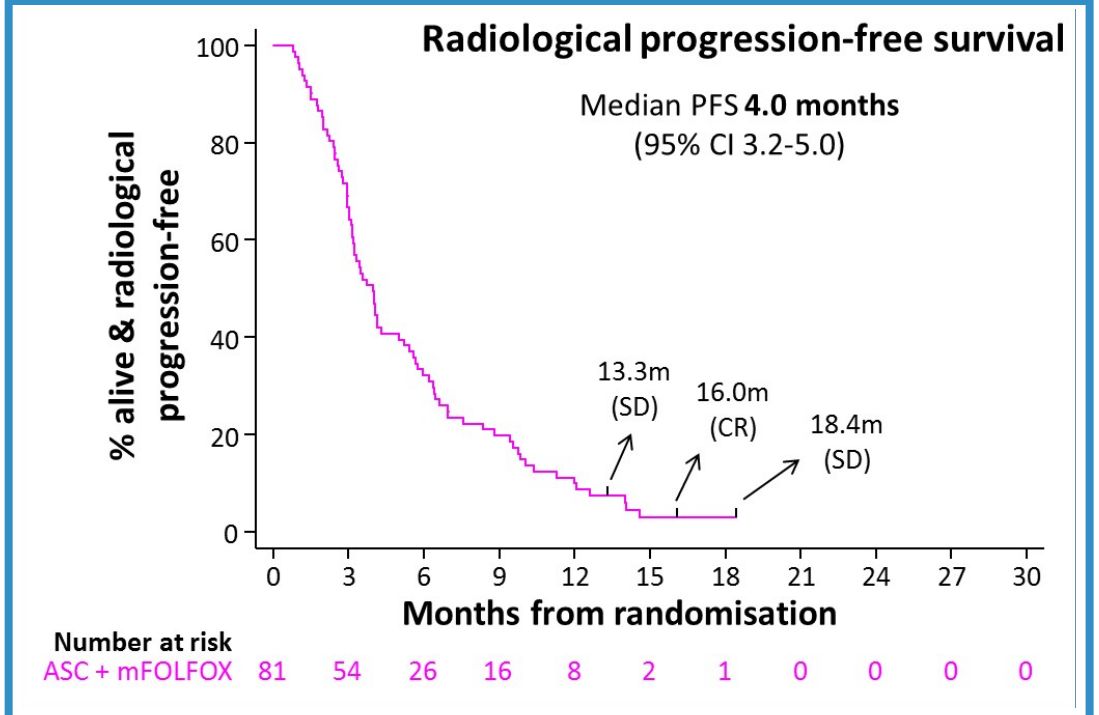
Phase 3 ABC-06 Active Symptom Control (ASC) vs. ASC + mFOLFOX evaluates the benefit of chemotherapy after GemCis

Overall survival by trial arm



	Arm A (ASC alone)	Arm B (ASC + mFOLFOX)
Adjusted* Hazard Ratio	**0.69** (95% CI 0.50-0.97) p=0.031	
Median OS	5.3 months	6.2 months
6-month survival-rate	35.5%	50.6%
12-month survival-rate	11.4%	25.9%

Radiological progression-free survival



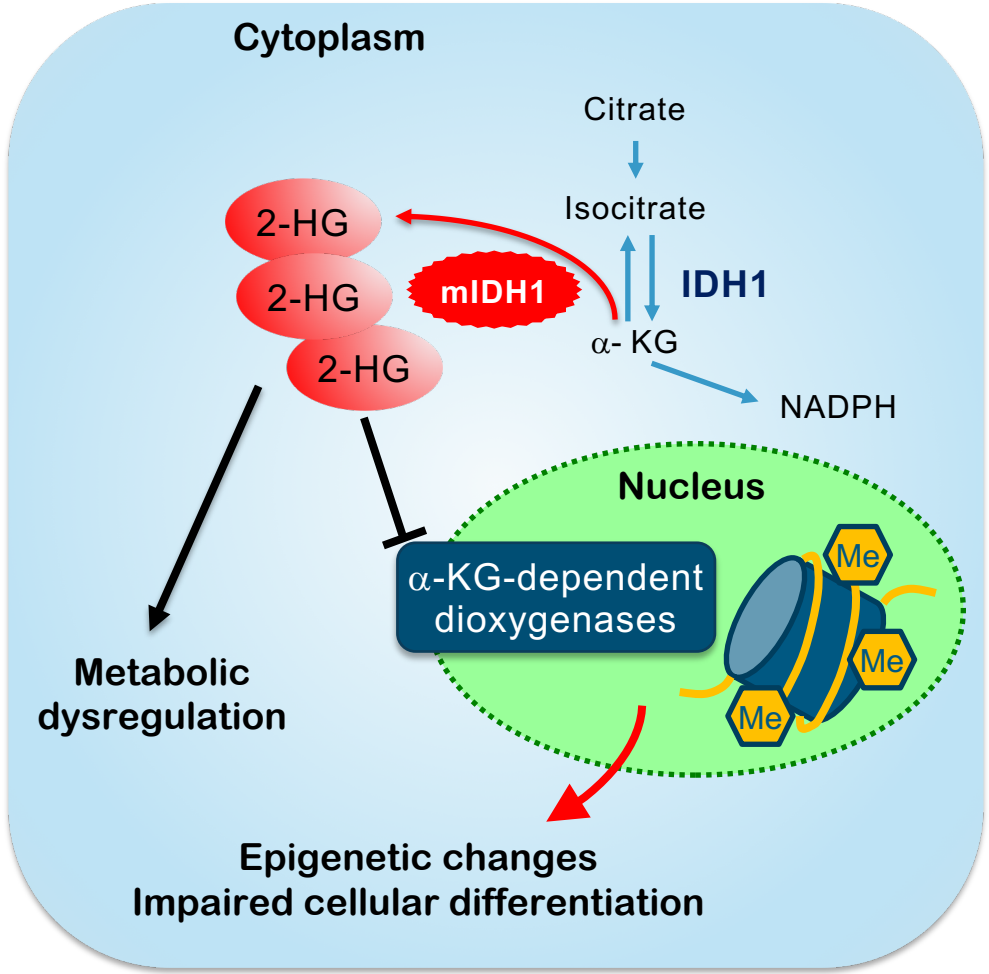
Source: Advanced Biliary Cancer (ABC) Working Group ASCO 2019 Presentation

ClarIDHy: A global, phase 3, randomized, double-blind study of ivosidenib vs placebo in patients with advanced cholangiocarcinoma with an IDH1 mutation

Andrew X. Zhu, M.D., Ph.D., Professor of Medicine at Harvard Medical School and Attending Oncologist at Massachusetts General Hospital

IDH1 mutations in advanced cholangiocarcinoma

- Advanced cholangiocarcinoma is an aggressive rare cancer with treatment options limited primarily to chemotherapy[1]
- IDH1 mutations occur in up to 20% of cholangiocarcinoma and do not confer a favorable prognosis[1]
- Ivosidenib (AG-120) is a first-in-class, oral, targeted, small-molecule inhibitor of the mutant IDH1 (mIDH1) protein,[2] and is FDA-approved for mIDH1 R/R AML and ND AML not eligible for intensive chemotherapy[3]
- A phase 1 study of ivosidenib included 73 previously treated mIDH1 cholangiocarcinoma patients and was associated with: median PFS, 3.8 months; 6- and 12-month PFS rates, 40.1% and 21.8%, respectively; and median OS 13.8 months[4]



2-HG=D-2-hydroxyglutarate; α-KG=alpha-ketoglutarate; AML=acute myeloid leukemia; FDA=Food and Drug Administration; Me=methyl groups; ND=newly-diagnosed; OS=overall survival; PFS=progression-free survival; R/R=relapsed/refractory.

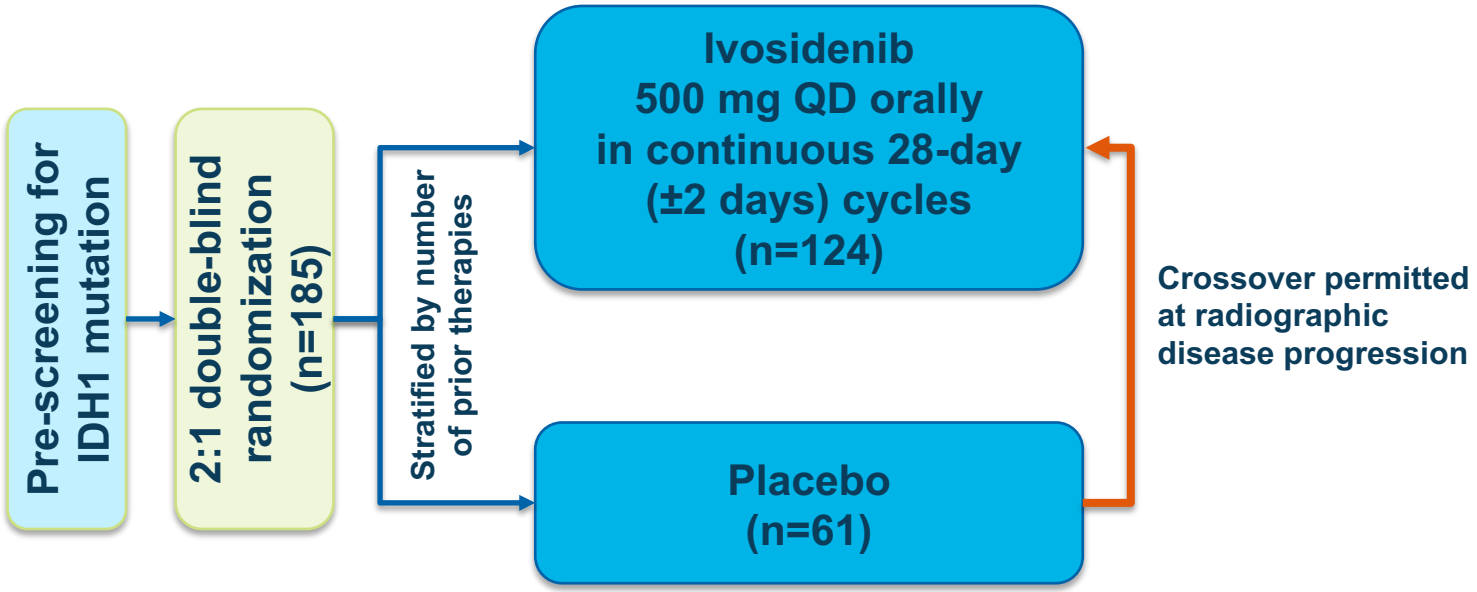
1. Boscoe AN, et al. *J Gastrointest Oncol*. 2019;10:751-765. **2.** Popovici-Muller J, et al. *ACS Med Chem Lett*. 2018;9:300-305. **3.** TIBSOVO highlights of prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211192s001lbl.pdf. Accessed August 5, 2019. **4.** Lowery MA, et al. *Lancet Gastroenterol Hepatol*. 2019;4:711-720.

ClarIDHy: Study design and endpoints

Key eligibility criteria

- ≥18 years of age
- Histologically confirmed diagnosis of cholangiocarcinoma
- Centrally confirmed mIDH1* status by NGS
- ECOG PS score 0 or 1
- 1-2 prior therapies (at least 1 gemcitabine- or 5-FU-containing regimen)
- Measurable lesion as defined by RECIST v1.1
- Adequate hematologic, hepatic, and renal function

NCT02989857



An independent data monitoring committee monitored the safety data throughout the study

- **Primary endpoint:** PFS by blinded independent radiology center (IRC)
- **Secondary endpoints included:** safety and tolerability; PFS by local review; OS; objective response rate; quality of life (QoL)†; pharmacokinetics/pharmacodynamics
- Sample size of ~186 patients based on hazard ratio (HR)=0.5, 96% power, 1-sided alpha=0.025
- 780 patients were screened for IDH1 mutations across 49 sites and 6 countries

*IDH1 mutation status prospectively confirmed by NGS-based Oncomine™ Focus Assay on formalin-fixed, paraffin-embedded tumor tissue in a Clinical Laboratory Improvement Amendments-certified laboratory.

†Assessed using EQ-5D-5L, EORTC QLQ-C30, EORTC QLQ-BIL21, and PGI questions.

ECOG PS=Eastern Cooperative Oncology Group Performance Status; EORTC=European Organisation for Research and Treatment of Cancer; EQ-5D-5L=5-level EuroQoL-5 Dimension questionnaire; FU=fluorouracil; NGS=next-generation sequencing; PGI=Patient Global Impression; QD=once daily; QLQ-BIL21=Cholangiocarcinoma and Gallbladder Cancer module; QLQ-C30=Quality of Life Questionnaire Core 30; RECIST=Response Evaluation Criteria in Solid Tumors.

ClarIDHy: Patient disposition

	Ivosidenib (n=124)	Placebo (n=61)
Treated, n (%)	121 (97.6)	59 (96.7)
On treatment	38 (31.4)	8 (13.6)
Discontinued treatment	83 (68.6)	51 (86.4)
Progressive disease	65 (53.7)	44 (74.6)
Adverse events	6 (5.0)	4 (6.8)
Death	4 (3.3)	0
Withdrawal by patient	6 (5.0)	2 (3.4)
Withdrawal of consent	1 (0.8)	1 (1.7)
Other	1 (0.8)	0
Not treated, n (%)	3 (2.4)	2 (3.3)
On study, n (%)	71 (57.3)	27 (44.3)

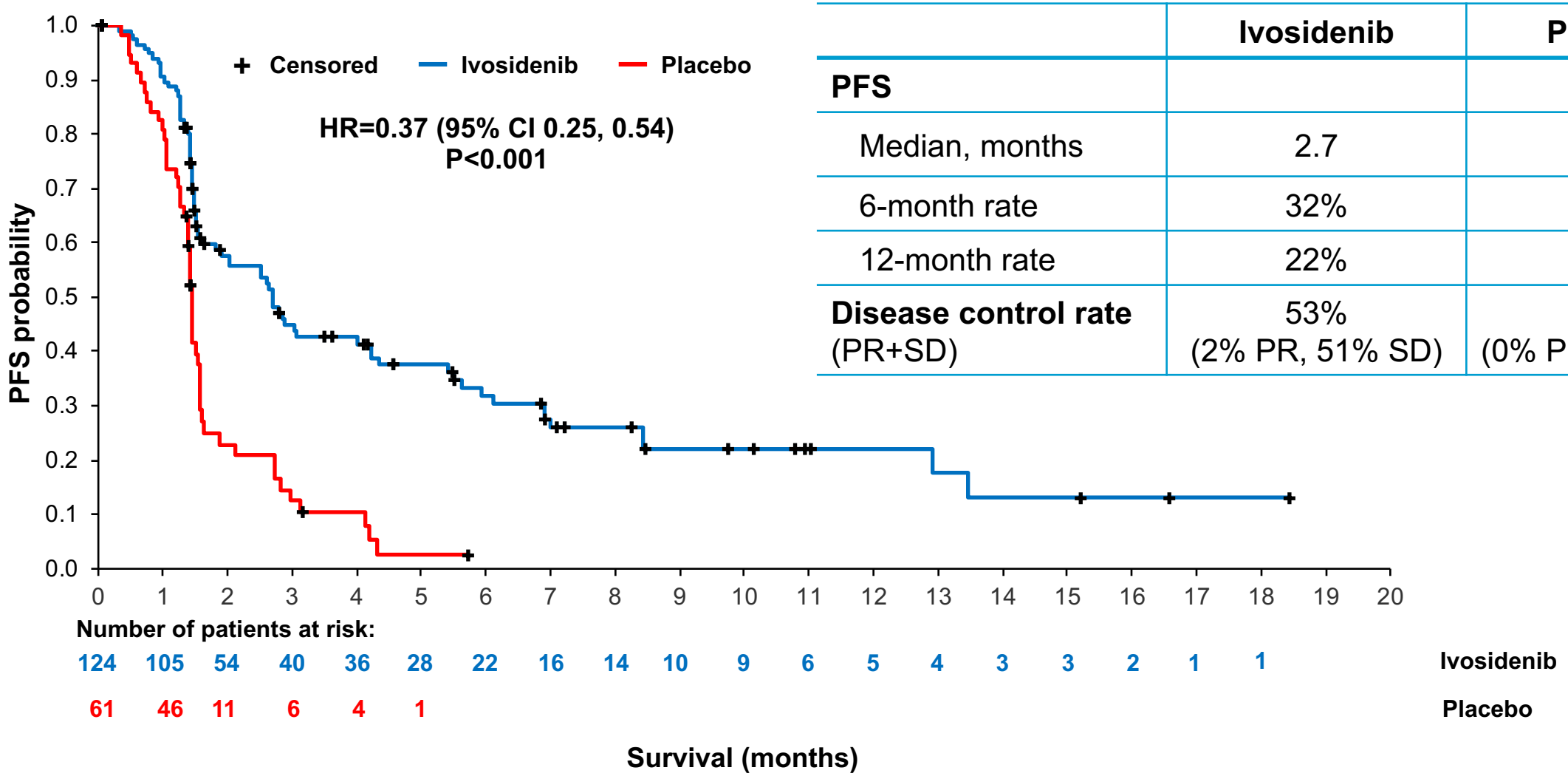
- As of the January 31, 2019 data cut, 35 placebo-treated patients (57.4%) crossed over to open-label ivosidenib upon radiographic disease progression and unblinding
- 26 placebo-treated patients (42.6%) did not cross over due to the following reasons: death (n=13), still on placebo treatment (n=8), never dosed (n=2), withdrawal of consent (n=2), received another treatment (n=1)

ClarIDHy: Baseline characteristics

Characteristic	Ivosidenib (n=124)	Placebo (n=61)
Randomization strata, n (%)		
1 prior line of therapy	66 (53.2)	33 (54.1)
2 prior lines of therapy	58 (46.8)	28 (45.9)
IDH1 mutation, n (%)		
R132C	84 (67.7)	45 (73.8)
R132L/G/S/H	21 (16.9); 17 (13.7); 2 (1.6); 0	7 (11.5); 6 (9.8); 1 (1.6); 2 (3.3)
ECOG PS score at baseline,* n (%)		
0	49 (39.5)	19 (31.1)
1	74 (59.7)	41 (67.2)
Cholangiocarcinoma type at diagnosis, n (%)		
Intrahepatic	111 (89.5)	58 (95.1)
Extrahepatic/Perihilar	5 (4.0)	1 (1.6)
Unknown	8 (6.5)	2 (3.3)
Extent of disease at screening		
Local/regional	9 (7.3)	5 (8.2)
Metastatic	115 (92.7)	56 (91.8)

*Two (2) patients had an ECOG worsen to 2 (placebo) and 3 (ivosidenib) at baseline assessment upon study start.

ClarIDHy: PFS by IRC



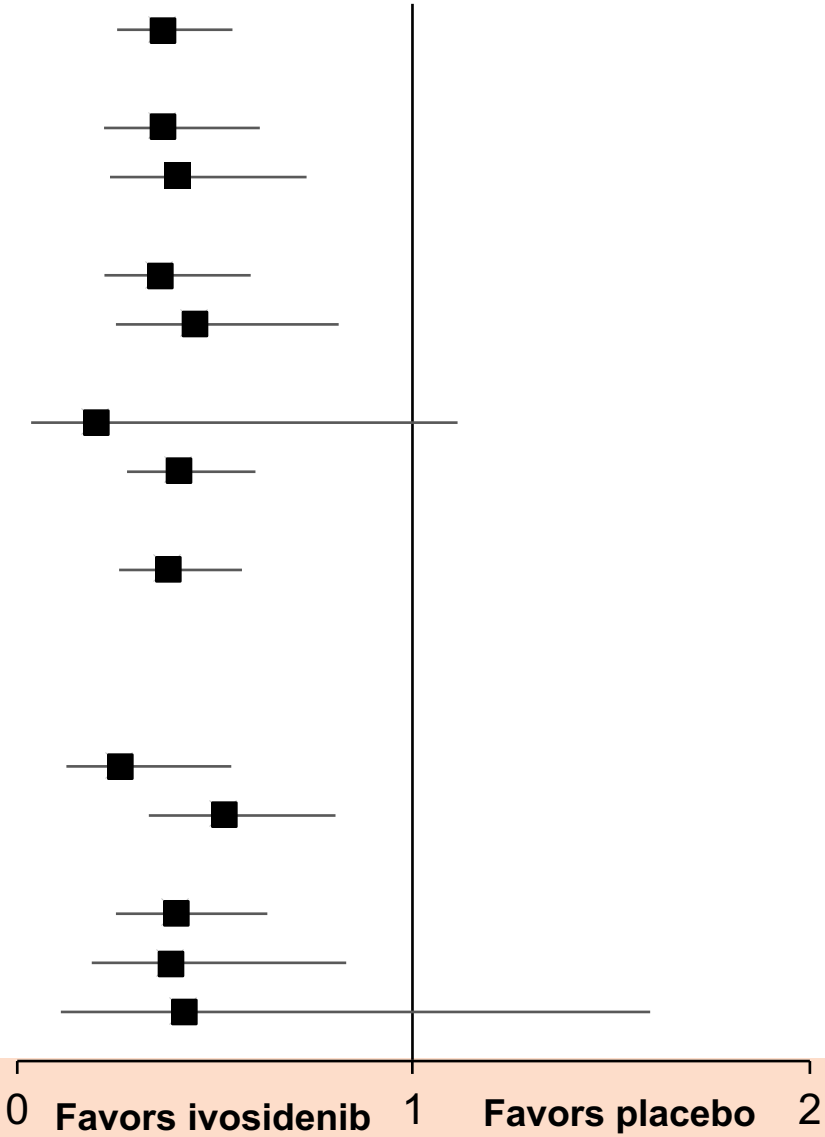
	Ivosidenib	Placebo
PFS		
Median, months	2.7	1.4
6-month rate	32%	NE
12-month rate	22%	NE
Disease control rate (PR+SD)	53% (2% PR, 51% SD)	28% (0% PR, 28% SD)

NE=not estimable; PR=partial response; SD=stable disease.

ClarIDHy: Ivosidenib efficacy consistent across subgroups*

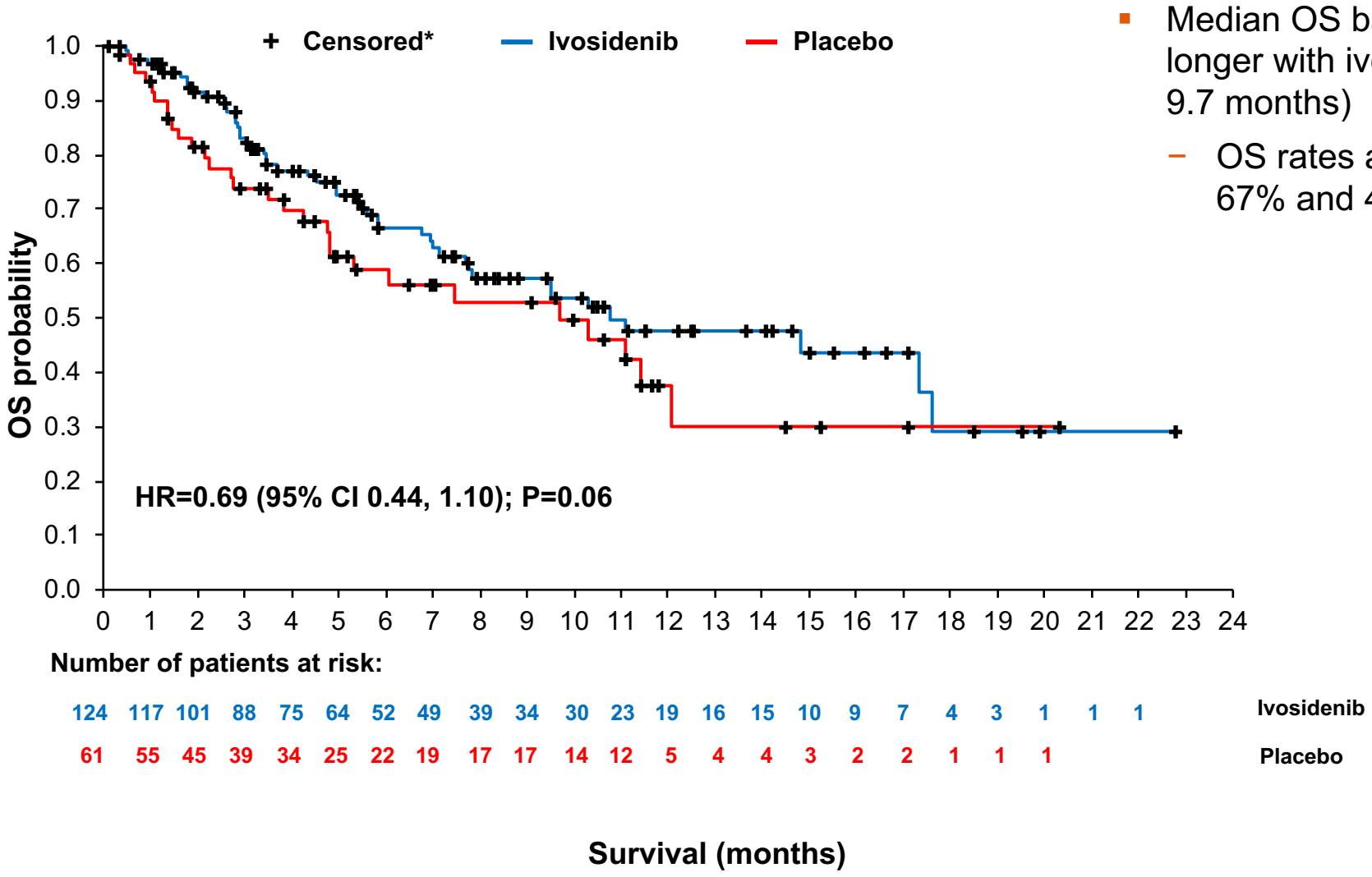
PFS by IRC

	Events/N	HR	Lower 95% CI	Upper 95% CI
Overall	126/185	0.37	0.252	0.543
Prior lines of therapy				
1	66/106	0.37	0.219	0.612
≥2	60/79	0.41	0.234	0.730
Gender				
Female	74/117	0.36	0.220	0.589
Male	52/68	0.45	0.249	0.811
Extent of disease at screening				
Locally advanced	7/14	0.20	0.035	1.111
Metastatic	119/171	0.41	0.277	0.601
Cancer type at initial diagnosis				
Intrahepatic cholangiocarcinoma	114/169	0.38	0.257	0.567
extrahepatic cholangiocarcinoma	3/6			
unknown	9/10			
ECOG PS score at baseline				
0	41/68	0.26	0.124	0.540
≥1	85/117	0.52	0.332	0.803
Regions				
North America	83/124	0.40	0.249	0.631
Europe	34/49	0.39	0.188	0.830
Asia	9/12	0.42	0.110	1.597



*Subgroups with events number ≤10 were not plotted.

ClarIDHy: OS by intent-to-treat (ITT)

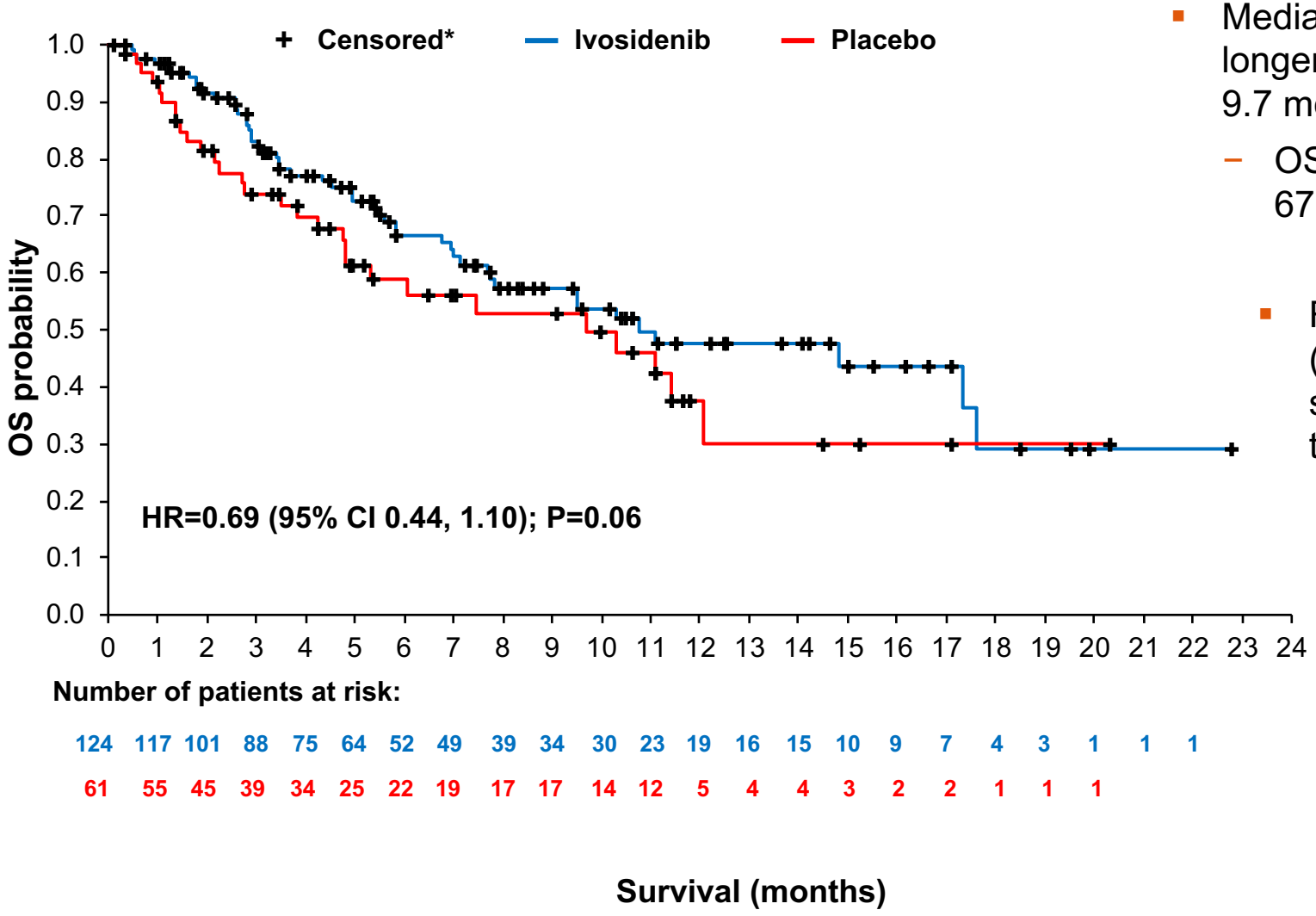


- Median OS based on 78 events was numerically longer with ivosidenib than placebo (10.8 vs. 9.7 months)
  - OS rates at 6 and 12 months for ivosidenib: 67% and 48% vs. 59% and 38% for placebo

*Patients without documentation of death at the data cutoff date were censored at the date the patient was last known to be alive or the data cutoff date, whichever was earlier.

1. Watkins C, et al. *Pharm Stat*. 2013;12:348-357. **2.** Robins JM, Tsiatis AA. *Commun Stat Theory Methods*. 1991;20:2609-2631.

ClarIDHy: OS by intent-to-treat (ITT)



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- Rank-preserving structural failure time (RPSFT)[1,2] method used to reconstruct the survival curve for the placebo subjects as if they had never crossed over to ivosidenib

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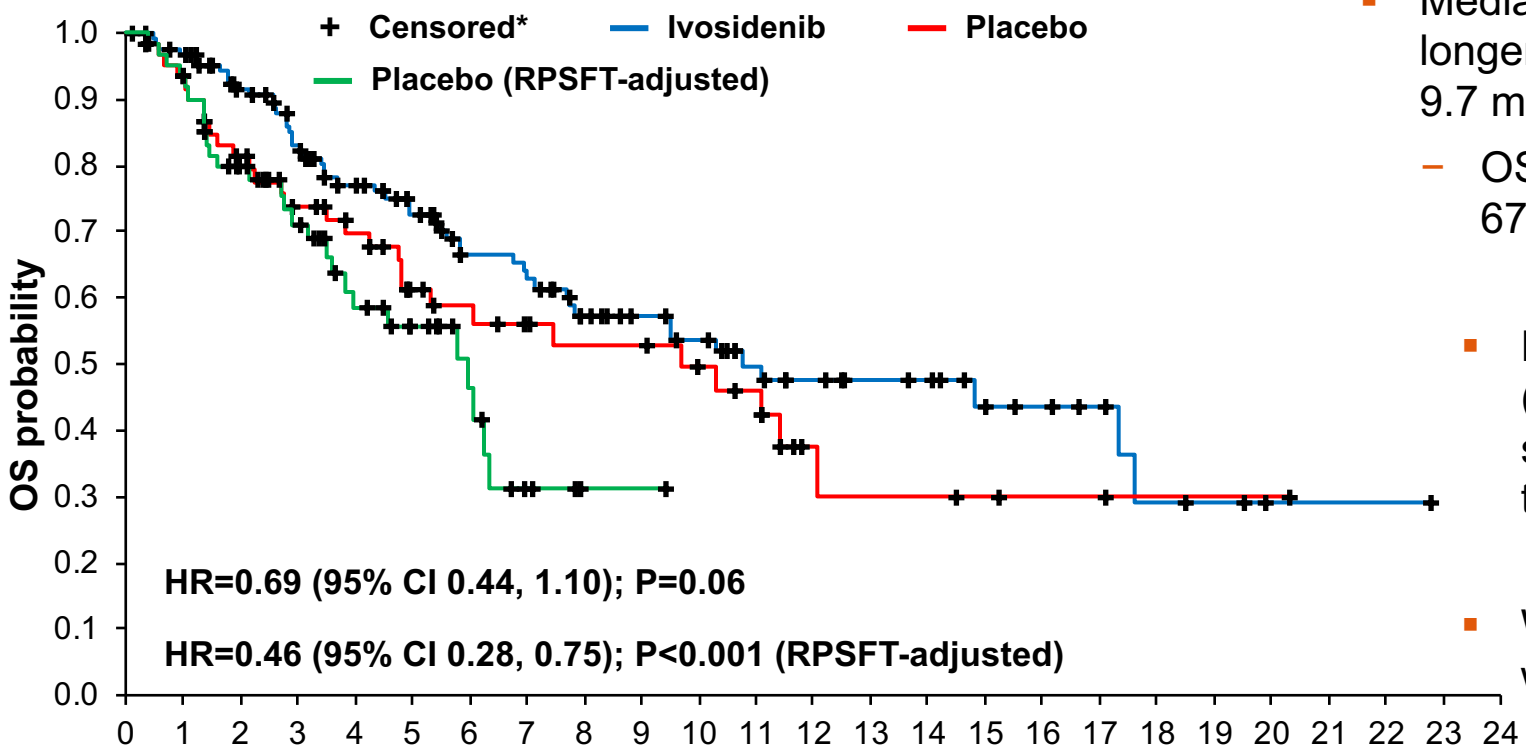

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- Rank-preserving structural failure time (RPSFT)[1,2] method used to reconstruct the survival curve for the placebo subjects as if they had never crossed over to ivosidenib
- With the RPSFT method, the median OS with placebo adjusts to 6 months

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1. Watkins C, et al. *Pharm Stat*. 2013;12:348-357. **2.** Robins JM, Tsiatis AA. *Commun Stat Theory Methods*. 1991;20:2609-2631.

ClarIDHy: Treatment-emergent adverse events (TEAEs)

	Placebo (n=59)	Ivosidenib (n=121)	Total ivosidenib (n=156)*
Any TEAE, n (%)	57 (96.6)	115 (95.0)	146 (93.6)
Most common TEAEs, n (%)			
Nausea	15 (25.4)	43 (35.5)	50 (32.1)
Diarrhea	9 (15.3)	37 (30.6)	45 (28.8)
Fatigue	10 (16.9)	32 (26.4)	37 (23.7)
Cough	5 (8.5)	25 (20.7)	30 (19.2)
Abdominal pain	8 (13.6)	26 (21.5)	29 (18.6)
Ascites	9 (15.3)	25 (20.7)	29 (18.6)
Decreased appetite	11 (18.6)	23 (19.0)	27 (17.3)
Anemia	3 (5.1)	18 (14.9)	25 (16.0)
Vomiting	10 (16.9)	23 (19.0)	25 (16.0)

- Grade ≥3 TEAE: 35.6% for placebo vs. 46.2% for total ivosidenib. Most common (placebo vs. total ivosidenib): ascites (6.8% vs. 7.7%), bilirubin increase (1.7% vs. 5.8%), anemia (0% vs. 5.1%), AST increase (1.7% vs. 5.1%)
- TEAEs leading to discontinuation were more common for placebo (8.5% vs. 5.8%) than total ivosidenib
- TEAEs leading to dose reductions (2.6% vs. 0%) and interruptions (26.3% vs. 16.9%) were more common for total ivosidenib relative to placebo

*Total ivosidenib includes 35 patients initially assigned to placebo who had crossed over to ivosidenib upon radiographic disease progression and unblinding.
>15% TEAEs based on total ivosidenib

ClarIDHy: QoL results

EORTC QLQ-C30 Physical Function Score, change from baseline at C2D1	Ivosidenib (n=62)	Placebo* (n=20)
Least square mean (SE)†	−3.4 (1.8)	−13.1 (3.0)
Difference (95% CI) vs. placebo	9.8 (2.8, 16.7)	–

- Change from baseline on physical functioning at C2D1‡ favored ivosidenib where placebo patients had a significantly larger (P=0.006§) and clinically meaningful decline in EORTC QLQ-C30 Physical Functioning score compared with ivosidenib patients
- Change from baseline on emotional functioning at C2D1‡ favored ivosidenib where placebo patients had worsened emotional functioning than ivosidenib patients based on EORTC QLQ-C30 Emotional Functioning and QLQ-BIL21 Anxiety symptom scores
- Data limited by small sample size at post-baseline time points

*Analyses focused on data from patients randomized to placebo, before crossover.
†Higher score is better.
‡Analyses focused on C2D1 considering the availability of QoL data.
§MMRM analysis of the change from baseline subscale score was applied, with baseline score, treatment, visit, and treatment-by-visit as fixed effects, and patient as random effect. Visit was treated as a categorical variable. Compound symmetry covariance matrix was used. P-value was not adjusted for multiplicity.
‖12- to 13-point score decrease estimated from anchor-based analyses represents clinically meaningful worsening.
C2D1=Day 1 of Cycle 2; MMRM=mixed-effect models with repeated measurements; SE=standard error.

Conclusions

- Ivosidenib significantly improved PFS relative to placebo (HR=0.37 [95% CI 0.25, 0.54]; P<0.001) in previously treated patients with mIDH1 advanced cholangiocarcinoma
- Ivosidenib resulted in a numerical improvement in OS compared with placebo based on ITT, and a significant improvement in OS vs. placebo when adjusting for crossover using the RPSFT method (HR=0.46 [95% CI 0.28, 0.75]; P<0.001)
- Ivosidenib 500 mg QD demonstrated a favorable safety profile
- Ivosidenib was associated with better physical and emotional functioning compared with placebo based on EORTC QLQ-C30 and QLQ-BIL21 QoL scores
- These pivotal data demonstrate the clinical relevance and benefit of ivosidenib in mIDH1 cholangiocarcinoma, and establish the role for genomic testing in this rare cancer with a high unmet need

Closing Remarks and Q&A

2019 Key Milestones & Data Presentations Position Agios for Long-term Value Creation

Key 2019 Milestones

- ✓ FDA approval and commercialization of monotherapy TIBSOVO® in untreated AML
- ✓ Initiate AG-636 Phase 1 dose-escalation trial in lymphoma in 1H 2019
- ✓ Complete AG-270 Phase 1 dose-escalation and select go forward dose
- ✓ Initiate expansion arms in the AG-270 Phase 1 study in Q3 2019
- Achieve proof-of-concept for mitapivat in thalassemia in 2H 2019
- Submit sNDA for TIBSOVO® in second line or later cholangiocarcinoma by YE
- Initiate glioma registration-enabling trial with vorasidenib by YE
- Complete enrollment in PK deficiency pivotal trials ACTIVATE-T and ACTIVATE by YE

Key Upcoming Data Presentations

- ✓ Presented full data from Phase 3 ClarIDHy trial of TIBSOVO® in IDH1m advanced cholangiocarcinoma at ESMO on Sept. 30
- Data from single agent dose-escalation portion of Phase 1 trial of AG-270 in MTAP-deleted tumors has been accepted for presentation at AACR-NCI-EORTC
- Data from IDH and PKR programs have been submitted for presentation at ASH, including:
  - New data from the extension phase of the Phase 2 DRIVE PK study of mitapivat in adults with PK deficiency
  - Important translational data from the Phase 1 study of TIBSOVO® and azacitidine in frontline AML