

**LBA10**

**Nal-IRI with 5-fluorouracil (5-FU) and leucovorin or gemcitabine plus cisplatin in advanced biliary tract cancer: Final results of the NIFE-trial (AIO-YMO HEP-0315), a randomized phase II study of the AIO biliary tract cancer group**

L. Perkhofer<sup>1</sup>, J.K. Striefler<sup>2</sup>, M. Sinn<sup>3</sup>, B. Opitz<sup>4</sup>, T.O. Goetze<sup>5</sup>, E. Gallmeier<sup>6</sup>, L. Fischer von Weikersthal<sup>7</sup>, L. Jacobasch<sup>8</sup>, D. Waldschmidt<sup>9</sup>, M. Niedermeier<sup>10</sup>, M. Sohm<sup>11</sup>, D. Sookthai<sup>5</sup>, A. Berger<sup>1</sup>, A. Beutel<sup>1</sup>, T. Seufferlein<sup>1</sup>, T.J. Ettrich<sup>1</sup>

<sup>1</sup> Department of Internal Medicine I, University of Ulm, Ulm, Germany, <sup>2</sup> Hematology, Oncology and Tumor Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, <sup>3</sup> Department of Oncology, Hematology and BMT with Division of Pneumology, UKE Universitätsklinikum Hamburg-Eppendorf KMTZ, Hamburg, Germany, <sup>4</sup> Medical Oncology, Hospital St. Elisabeth and St. Barbara Halle, Halle, Germany, <sup>5</sup> Institute of Clinical Cancer Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt am Main, Germany, <sup>6</sup> Department of Gastroenterology and Endocrinology, Philipps University Marburg, Marburg, Germany, <sup>7</sup> Praxis Dr. L. Fischer von W., Klinikum St. Marien Amberg, Amberg, Germany, <sup>8</sup> Oncology/Hematology Department, Gemeinschaftspraxis Haematologie - Onkologie, Dresden, Germany, <sup>9</sup> Klinik für Gastroenterologie und Hepatologie, Universitätsklinikum Köln (AöR), Cologne, Germany, <sup>10</sup> Oncology/Hematology, Private Practice Memmingen, Memmingen, Germany <sup>11</sup> SAPV, Praxis Dr. Vehling-Kaiser, Landshut, Germany

**Background**

Survival and treatment options in advanced biliary tract cancer (BTC) are limited with the current standard of care gemcitabine/cisplatin. The NIFE study examined nanoliposomal-irinotecan (nal-IRI)/5-FU/leucovorin (LV) as an alternative 1<sup>st</sup>-line treatment option in advanced BTC.

**Methods**

NIFE is a prospective, randomized, two-sided, phase II study. Advanced BTC patients were randomized (1:1) to receive either nal-IRI/5-FU/LV (arm A) or gemcitabine/cisplatin (arm B) with a stratification for tumor site (intrahepatic vs. extrahepatic), sex and ECOG (0 vs. 1). Arm A was planned as a Simon's optimal two-stage design and arm B served as an internal control for selection bias. As primary endpoint a 4 months (mo) progression free survival (PFS) rate ≥50% in the ITT-population was defined.

**Results**

Between 01/2018-09/2020 93 patients were randomly assigned in 21 German centers. Two patients violating inclusion criteria had to be excluded from the ITT population (n=91) due to inappropriate randomization. The NIFE trial met its primary endpoint with a PFS-rate of 51% at 4mo in the ITT population (arm A). Median PFS in arm A was 5.98mo (2.37-9.59) and in arm B 6.87mo (2.46-7.82). Provisional median overall survival (mOS) was 15.9mo (10.58-21.85) in arm A and 13.63mo (6.51-17.68) in arm B with ongoing follow-up at data closesure. Median PFS in intrahepatic (ICCA) vs. extrahepatic (ECCA) cholangiocarcinoma was 3.45mo (2.10-6.05) vs. 9.59mo (1.94-15.67) in arm A and 7.72mo (6.05-9.46) vs. 1.76mo (0.16-6.87) in arm B. Corresponding mOS times were ICCA 14.19/ECCA 18.23mo in arm A and ICCA 16.36/ECCA 6.34mo in arm B. Table: LBA10

	ITT (n=91)		Arm B (n=42) Gemcitabine/cisplatin	
	Arm A (n=49) Nal-IRI/5-FU/LV			
PFS rate at 4mo	51.0% ICCA (n=34)	41.2% ECCA (n=15)	59.5% ICCA (n=32)	71.9% ECCA (n=10)
mPFS	5.98mo (95% CI 2.37-9.59) ICCA (n=34)	3.45mo (95% CI 2.10-6.05) ECCA (n=15)	6.87mo (95% CI 2.46-7.82) ICCA (n=32)	7.72mo (95% CI 6.05-9.46) ECCA (n=10)
mOS	15.9mo (95% CI 10.58-21.85) ICCA (n=34)	14.19mo (95% CI 7.69-21.85) ECCA (n=15)	13.63mo (95% CI 6.51-17.68) ICCA (n=32)	16.36mo (95% CI 7.46-19.91) ECCA (n=10)
ORR	24.5%		11.9%	
DCR at 2mo	57.1%		57.1%	

ICCA: intrahepatic CCA, ECCA: Extrahepatic CCA, NE: not estimable

## Conclusions

In the phase II NIFE trial nal-IRI/5-FU/LV showed efficacy as 1<sup>st</sup>-line treatment of advanced BTC with no new safety findings. ECCA and ICCA responded differently to drug interventions, with a clear benefit for nal-IRI/5-FU/LV in ECCA.

## Clinical trial identification

AIO-YMO HEP-0315 (NIFE); EudraCT 2016-002467-34; NCT03044587.

## Legal entity responsible for the study

AIO-Studien GmbH.

## Funding

Servier.

## Disclosure

M. Sinn: Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Sanofi. T.O. Goetze: Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: MSD Sharp Dohme; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Celgene; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Invited Speaker: Lilly; Financial Interests, Personal, Invited Speaker: MCI; Financial Interests, Personal, Invited Speaker: MSD Sharp Dohme; Financial Interests, Personal, Research Grant: AstraZeneca; Financial Interests, Personal, Research Grant: Incyte; Financial Interests, Personal, Research Grant: Lilly. D. Waldschmidt: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: Celgene; Financial Interests, Personal, Advisory Board: Eisai; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Advisory Board: Falk; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: Shire Baxalta; Financial Interests, Personal, Advisory Board: Sirtex. T. Seufferlein: Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Pierre Fabre; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Baxalta; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Speaker's Bureau: Sanofi; Financial Interests, Personal, Speaker's Bureau: Pierre Fabre; Financial Interests, Personal, Speaker's Bureau: Pfizer; Financial Interests, Personal, Speaker's Bureau: Baxalta; Financial Interests, Personal, Speaker's Bureau: Servier; Financial Interests, Personal, Research Grant: Boehringer; Financial Interests, Personal, Research Grant: Sanofi; Financial Interests, Personal, Research Grant: Celgene; Financial Interests, Personal, Research Grant: Amgen. T.J. Ettrich: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Advisory Board: Sanofi Aventis; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Advisory Board: Pierre-Fabre Pharma; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Institutional, Research Grant: Servier; Financial Interests, Institutional, Research Grant: Sanofi Aventis; Financial Interests, Institutional, Research Grant: Celgene. All other authors have declared no conflicts of interest.

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