NUC-1031 in combination with cisplatin for first-line treatment of advanced biliary tract cancer

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Email: jennifer.knox@uhn.ca

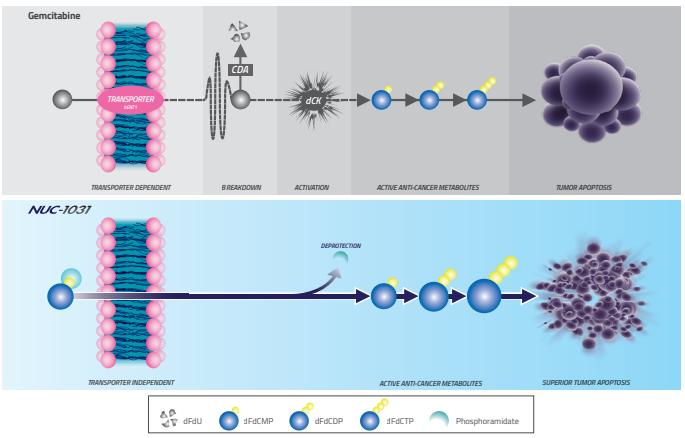
JJ Knox[1], MG McNamara[2,3], DH Palmer[4], TRJ Evans[5], J Bridgewater[6], JW Valle[2,3]

1) Princess Margaret Cancer Centre, Toronto, ON, Canada 2) Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK
3) University of Manchester, Division of Cancer Sciences, Manchester, UK 4) Clatterbridge Cancer Centre, Liverpool, UK
5) Beatson West of Scotland Cancer Centre, University of Glasgow, UK 6) University College London, London, UK

Background

- No approved agents exist for the treatment of locally advanced/metastatic biliary tract cancer (BTC)
- Current standard of care remains gemcitabine + cisplatin: OS 11.7 months (ABC-02)[1]
- Resistance to chemotherapy associated with poor survival prognosis
- Effective new agents and combinations are required

NUC-1031 bypasses the key cancer resistance pathways of gemcitabine



NUC-1031: The First Anti-Cancer ProTide

- A new class of anti-cancer agents
- ProTide transformation of gemcitabine
- Overcomes key gemcitabine resistance mechanisms[2]
  - Cellular uptake independent of nucleoside transporters (hENT1)
  - Activation independent of deoxycytidine kinase (dCK)
  - Protected from breakdown by cytidine deaminase (CDA)
- In comparison to gemcitabine, NUC-1031 has[3]
  - Greater plasma stability ($t^1/_2$ 8.3 hours vs 1.5 hours)
  - Increased intracellular levels of active anti-cancer metabolite, dFdCTP (217x)
  - Reduced toxic metabolites

ABC-08 Study (Phase Ib Study NUC-1031 + cisplatin)

Safety Profile

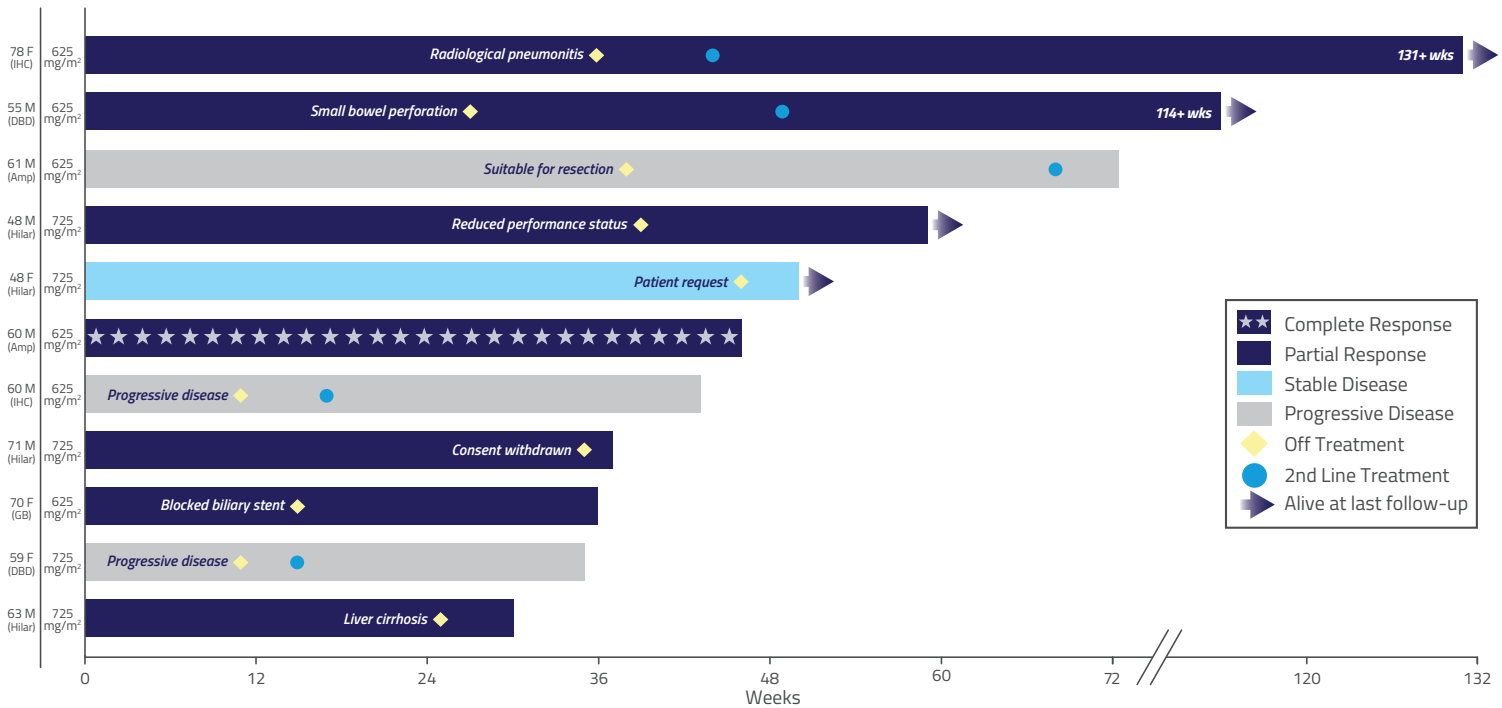
- NUC-1031 + cisplatin was well tolerated
  - No unexpected adverse events (AEs)
  - Multiple cycles administered (median 8; range 3.5-14)
- No dose-limiting toxicities (DLTs)
- Grade 3 AEs included: fatigue (21%), neutropenia (14%), pyrexia (14%), nausea (7%), and increased liver function enzymes (ALT; 14%, AST; 7%)
- No Grade 4 treatment-related AEs
- No patients discontinued due to NUC-1031 related events

Efficacy - Objective Response Rates in ABC-08 and ABC-02

	ABC-08 NUC-1031 + cisplatin	ABC-02[1] gemcitabine + cisplatin
	ITT	Evaluable
Complete Response	**7%** (1/14)	**0.6%** (1/161)
Partial Response	**43%** (6/14)	**25.5%** (41/161)
Objective Response Rate	**50%** (7/14)	**26.1%** (42/161)

Note: Responses unconfirmed in ABC-08 and ABC-02

Treatment duration and best overall response by BTC anatomic site of origin (Efficacy Evaluable Population, n=11)



NuTide:121 Study Design

Inclusion

- ≥18 years of age
- Histologically or cytologically-confirmed adenocarcinoma of the biliary tract (intra and extra-hepatic cholangiocarcinoma, gallbladder, or ampullary cancers) that is locally advanced, unresectable or metastatic
- Life expectancy ≥16 weeks
- ECOG performance status 0 or 1
- Adequate biliary drainage with no evidence of ongoing infection

R

NUC-1031 725mg/m² + cisplatin 25mg/m²

gemcitabine 1000mg/m² + cisplatin 25mg/m²

Dosing on Day 1+8 on q21d
9-weekly radiographic scanning

Primary Objectives
OS
ORR

Secondary Objectives
PFS PK
DOR QoL
Safety

Randomization Strata
- Measurable disease at baseline
- Metastatic disease at baseline
- Anatomic site of disease
- Geography

Enrollment → *Treatment* → *Endpoints*

Summary

- NUC-1031 + cisplatin shows encouraging efficacy compared to standard of care
- All BTC subtypes sensitive to NUC-1031 + cisplatin
- Durable responses
- NUC-1031 + cisplatin is well-tolerated over multiple cycles in patients with BTC
- NuTide:121 is a global phase III study that will be conducted at ~100 sites across North America, Europe and Asia-Pacific
- NUC-1031 + cisplatin has the potential to improve survival outcomes in patients with BTC
- For further study information contact: NuTide121@nucana.com

References: 1. Valle *et al. N Engl J Med* 2010; 362:1273-1281. 2. Slusarczyk *et al. J Med Chem* 2014; 57:1531-1542. 3. Blagden *et al. Br J Cancer* 2018; 119:815-822.

DBD: Distal bile duct IHC: Intrahepatic cholangiocarcinoma Hilar: Hilar cholangiocarcinoma GB: Gallbladder Amp: Ampullary

ABC-08 data current as of Aug 30 2018. Data cleaning ongoing.