

Phase III study of NUC-1031 + cisplatin vs gemcitabine + cisplatin for first-line treatment of patients with advanced biliary tract cancer

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BACKGROUND

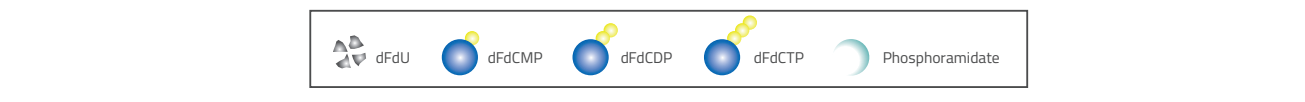
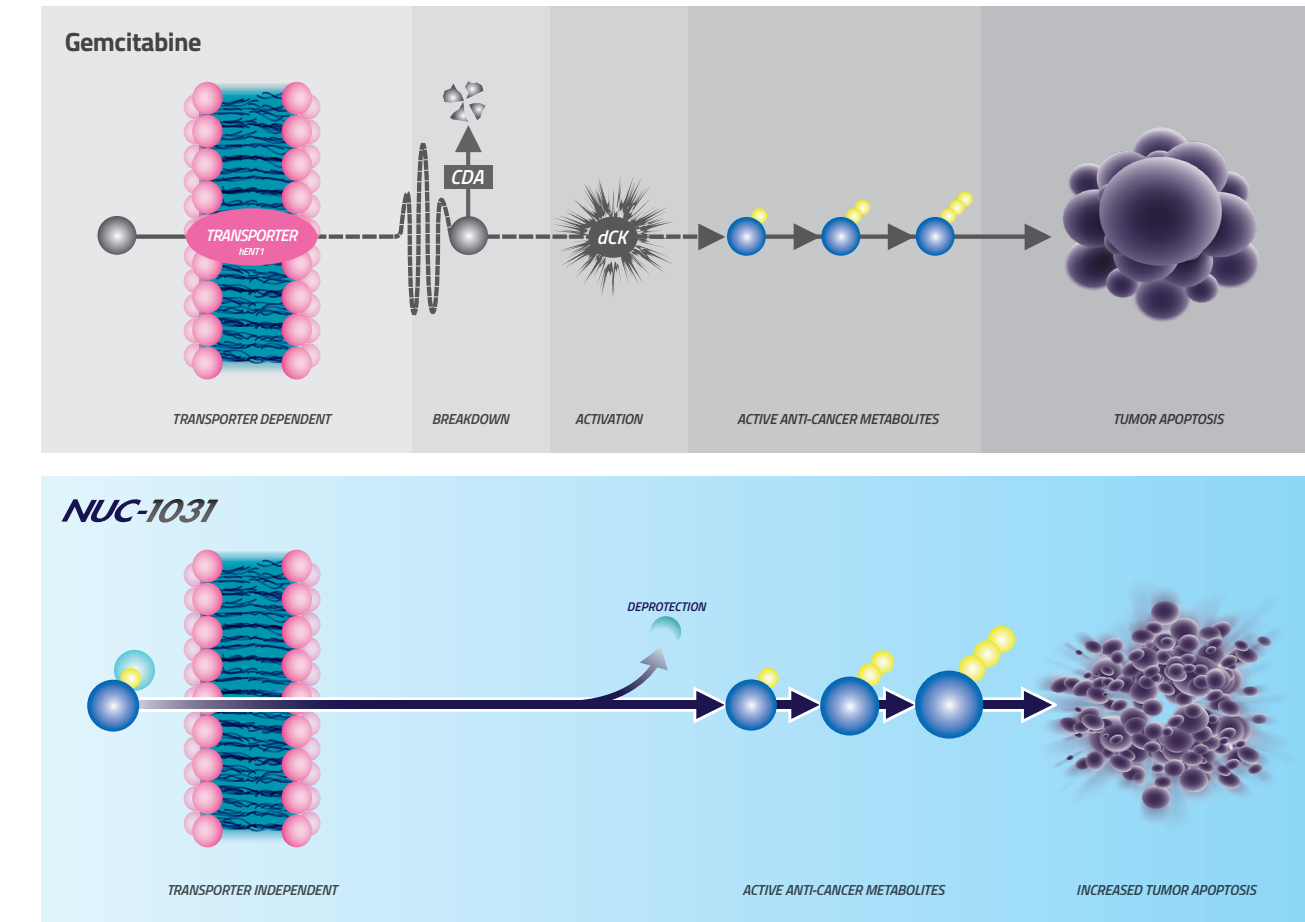
Biliary Tract Cancer (BTC)

- Aggressive cancer with a poor prognosis
- Heterogenous disease consisting of distinct subgroups
 - Intra and extra-hepatic cholangiocarcinoma, gallbladder, or ampullary
- No approved agents exist for the first-line treatment of advanced BTC
- Current standard of care: gemcitabine + cisplatin
 - Median overall survival (OS) 11.7 months (ABC-02)¹
- Resistance to chemotherapy is associated with poor survival
- Effective new agents and combinations are required

NUC-1031: A ProTide transformation of gemcitabine

- A new class of anti-cancer agents
- Overcomes key gemcitabine resistance mechanisms²
 - 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 has³:
 - 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

NUC-1031 bypasses the key cancer resistance pathways of gemcitabine



Phase 1b ABC-08 study: NUC-1031 + cisplatin⁴

- Favorable safety profile that was tolerated over multiple cycles;
- Encouraging efficacy with activity across all BTC subtypes (44% ORR*)

* Efficacy evaluable patients

NuTide 121

INCLUSION CRITERIA

- Previously untreated 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
- ≥18 years of age
- Life expectancy ≥16 weeks
- ECOG PS 0 or 1
- Adequate biliary drainage with no evidence of ongoing infection

RANDOMIZATION STRATA

- Measurable Disease
- Metastatic Disease
- Anatomic Site of Disease
- Geography

NUC-1031
725 mg/m²
+
cisplatin
25 mg/m²
dosing on days 1 & 8
of a 21-day cycle

gemcitabine
1000 mg/m²
+
cisplatin
25 mg/m²
dosing on days 1 & 8
of a 21-day cycle

PRIMARY ENDPOINTS

- OS
- ORR

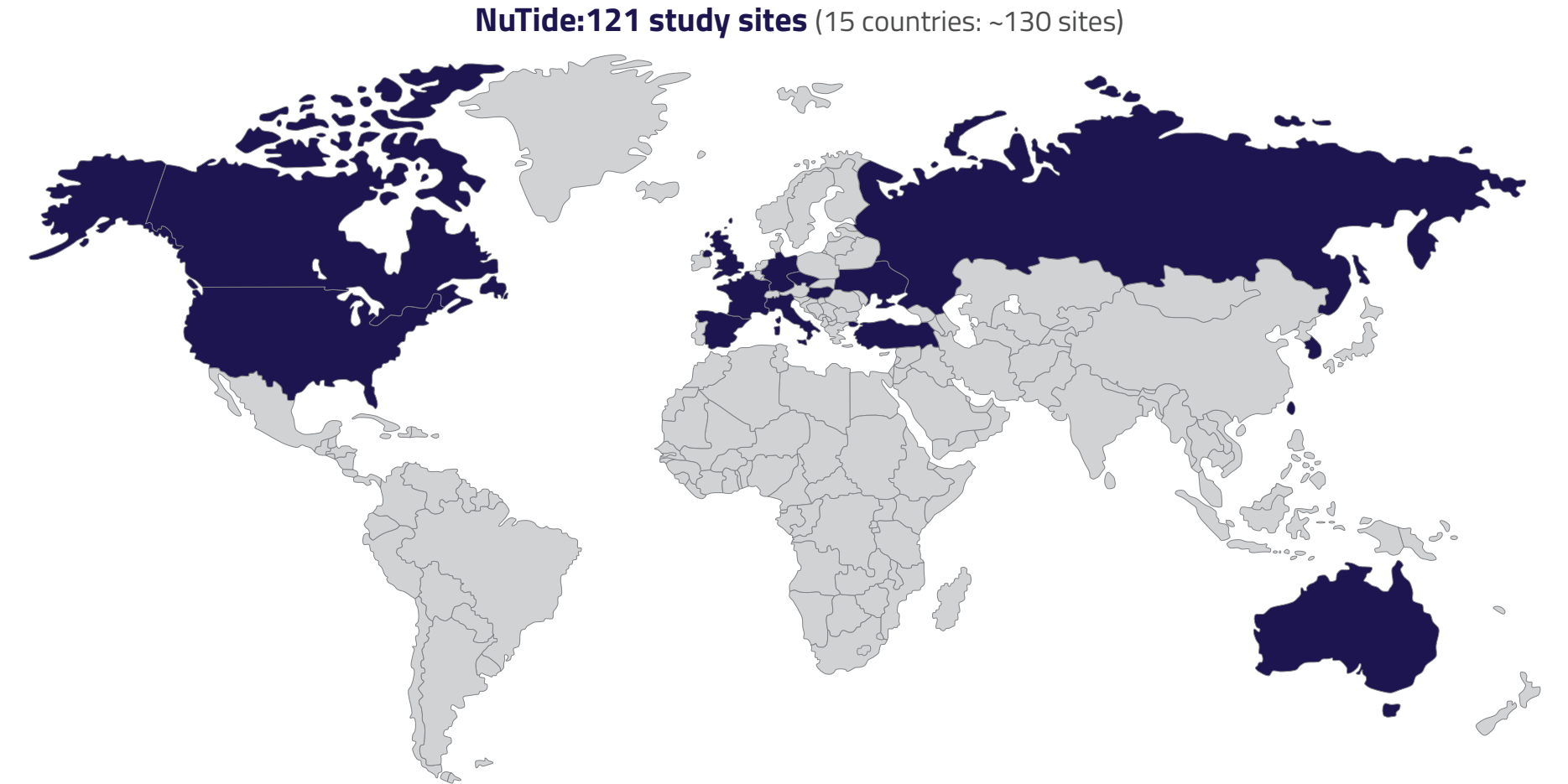
SECONDARY ENDPOINTS

- PFS
- DoR
- Safety
- PK
- QoL

NuTide:121 (Statistical Plan)

RECRUITMENT	FOLLOW UP	FINAL ANALYSIS	
<i>Accelerated Approval</i> <small>Interim 1 or 2 designed to support</small>			
	<i>Regular Approval</i> <small>Interim 2, 3 or 4 designed to support</small>		
Interim 1	Interim 2	Interim 3	Final
ORR 418 evaluable patients DIP ≥14%*	ORR 644 evaluable patients DIP ≥9%*	OS ~541 events DIM ≥2.6m*	Final OS ~637 events DIM ≥2.2m*

* DIP = Difference in observed proportions (vs. an estimated 19.0%) for statistical significance. Measurable disease at baseline and ≥28 weeks follow-up.
* DIM = Difference in observed medians (vs. an estimated 11.7 months) for statistical significance.



SUMMARY

- Global Phase III study at ~130 sites across North America, Europe and Asia-Pacific
- NUC-1031 + cisplatin has the potential to improve survival outcomes in patients with BTC
- Further study information: NuTide121@nucana.com