JAMA Oncology | Original Investigation

Nab-Paclitaxel and Gemcitabine as First-line Treatment of Advanced or Metastatic Cholangiocarcinoma
A Phase 2 Clinical Trial

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IMPORTANCE Gemcitabine with platinum has limited efficacy for treatment of advanced cholangiocarcinoma, necessitating an evaluation of alternative drug combinations. Recent evidence suggests that paclitaxel may potentiate gemcitabine activity.

OBJECTIVE To evaluate whether gemcitabine plus nanoparticle albumin-bound (nab)–paclitaxel is safe and effective for treatment of advanced cholangiocarcinoma.

DESIGN, SETTING, AND PARTICIPANTS This single-arm, 2-stage, phase 2 clinical trial was conducted at 23 community and academic centers across the United States and Europe. Patients aged 18 years or older enrolled between September 2014 and March 2016 had confirmed advanced or metastatic cholangiocarcinoma without prior systemic therapy, and had an Eastern Cooperative Oncology Group Performance Status score of 0 to 1 and a Child-Pugh score less than 8. Previous surgery, radiation, or liver-directed therapies were permitted.

INTERVENTIONS Patients received intravenous nab-paclitaxel, 125 mg/m^2, followed by gemcitabine, 1000 mg/m^2, on days 1, 8, and 15 of each 28-day treatment cycle until disease progression or unacceptable toxic effects.

MAIN OUTCOMES AND MEASURES The primary outcome was improvement in 6-month progression-free survival (PFS) rate (null and alternative hypotheses of 55% and 70%, respectively) in the evaluable population. Secondary outcomes included median overall survival (OS), PFS, time to progression, best overall response rate, disease control rate, safety and toxicity, and association of change in carbohydrate antigen 19-9 with survival.

RESULTS Seventy-four patients with a median age of 62 (range, 36-87) years, including 44 women (60%), were enrolled. Patients received a median of 6 (range, 1-18) treatment cycles, and the median follow-up was 10.2 (range, 0.6-27.3) months. The observed 6-month PFS rate of 61% (95% CI, 48%-73%) did not favor the alternative hypothesis. Median PFS was 7.7 (95% CI, 5.4-13.1) months, median OS was 12.4 (95% CI, 9.2-15.9) months, and median time to progression was 7.7 (95% CI, 6.1-13.1) months. The confirmed best overall response rate and disease control rate were 30% and 66%, respectively. Hazard ratios for an association between a change in serum carbohydrate antigen 19-9 and median PFS as well as median OS were 2.02 (95% CI, 0.86-4.75) (P = .10) and 1.54 (95% CI, 0.64-3.71) (P = .34), respectively. The most common treatment-related hematologic and nonhematologic adverse events at grade 3 or higher were neutropenia (43%) and fatigue (14%), respectively.

CONCLUSIONS AND RELEVANCE Although the trial did not meet its primary efficacy end point, the results indicate that a nab-paclitaxel plus gemcitabine regimen was well tolerated and may be an alternative option to current therapeutic approaches for advanced cholangiocarcinoma.

TRIAL REGISTRATION ClinicalTrials.gov identifier: NCT02181634

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Supplemental content

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The incidence of cholangiocarcinoma (CCA), classified as intrahepatic and extrahepatic (perihilar and distal), is increasing globally, including in the United States.[1] Advanced CCAs are aggressive cancers with a median survival in patients of less than 12 months.[2] The options for systemic therapy are limited, with a 5-year overall survival (OS) rate of approximately 5% despite treatment.[3] The standard first-line systemic therapy of gemcitabine and a platinum analogue for advanced unresectable and metastatic CCA has limited efficacy, necessitating an evaluation of alternative drug combinations.[2,4]

Paclitaxel can inhibit the gemcitabine-metabolizing enzyme cytidine deaminase to increase the intratumoral concentration of the active metabolites of gemcitabine.[5] Standard paclitaxel has considerable toxicity compared with the nanoparticle albumin-bound (nab) colloidal formulation, nab-paclitaxel (nabP), which has less vehicle-related hypersensitivity reactions, neurotoxicity, and neutropenia.[6-8] On the basis of preclinical evidence of the potential synergism and clinical efficacy of nabP and gemcitabine in treating breast and pancreatic cancer,[9-11] we conducted a phase 2, single-arm trial to assess the safety and efficacy of nabP and gemcitabine therapy for patients with advanced or metastatic CCA.

Key Points

Question Is nanoparticle albumin-bound (nab)–paclitaxel plus gemcitabine safe and effective for treating adult patients with advanced cholangiocarcinoma?

Findings In this single-arm, phase 2 clinical trial, intravenous treatment with nab-paclitaxel, 125 mg/m^2, and gemcitabine, 1000 mg/m^2, on days 1, 8, and 15 of every 28 days was well tolerated. The primary trial end point of 6-month progression-free survival rate of 61% failed to reject the null hypothesis of 55%, although the efficacy of this regimen may be similar to the standard chemotherapy regimens in cholangiocarcinoma.

Meaning This regimen has a tolerable safety profile and may be considered an acceptable alternative option for treating patients with advanced or metastatic cholangiocarcinoma.

Methods

Study Design

This was a phase 2, single-arm, 2-stage clinical trial (protocol No. PrE0204) with a planned enrollment of 70 patients to obtain 67 evaluable patients (trial protocol in Supplement 1). In stage 1, 35 evaluable patients were planned for, and if at least 21 patients were alive and progression free at 6 months, stage 2 would commence by enrolling an additional 32 evaluable patients. Stage 2 enrollment was permitted before the completion of the 6-month follow-up in stage 1 in the absence of significant grade 3 or higher toxic effects. The study protocol was approved by the ethics committee or institutional review board at each site. The study was conducted in accordance with the Declaration of Helsinki[12] and with the Good Clinical Practice Guidelines of the International Conference on Harmonization. Participating study sites and the PrECOG, LLC (Philadelphia, Pennsylvania) data safety monitoring board reviewed the safety data. All patients provided written informed consent before enrollment.

Outcomes

The primary outcome of the present study was the clinical efficacy of nabP plus gemcitabine therapy as determined by assessing improvement in the 6-month progression-free survival (PFS) rate. Secondary outcomes included evaluation of the median OS, PFS, and time to progression (TTP) rates and the best overall response rate (ORR) and disease control rate (DCR); the safety and toxicity profile of the treatment regimen; and the association of the maximum change in serum carbohydrate antigen 19-9 (CA19-9) level with survival. Exploratory outcomes, including enumeration of circulating tumor cells[13] and immunohistochemical evaluation of cytidine deaminase, human equilibrative nucleoside transporter 1,[13] and secreted protein acidic and rich in cysteine[14] protein expression levels, are pending and will be reported in a future article.

Patient Eligibility

Key patient eligibility requirements included being 18 years of age or older; pathologic confirmation of CCA, advanced or metastatic stage; no prior systemic therapy, disease radiographically measurable per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; an Eastern Cooperative Oncology Group Performance Status score of 0 to 1; and a Child-Pugh score less than 8. Previous surgery, radiation, or liver-directed therapies were permitted.

Investigational Treatment

On days 1, 8, and 15 of each 28-day treatment cycle, patients received intravenous nabP, 125 mg/m^2, followed by intravenous gemcitabine, 1000 mg/m^2, each for 30 minutes. Treatment was permitted until disease progression or development of an unacceptable toxic effect.

Assessments and Study End Points

To evaluate treatment response, computed tomography or magnetic resonance imaging was performed at baseline and every 8 weeks, and response assessment was defined per RECIST, version 1.1.[15,16] Serial serum CA19-9 level measurements were performed at baseline and every 8 weeks thereafter.

The PFS was calculated from the date of the first study treatment to either the date of documented disease progression or death from any cause, whichever occurred first. The OS was defined as the time from enrollment until death or censored at last patient contact. The TTP was calculated from date of first study treatment to date of disease progression. Among patients with a baseline serum CA19-9 level of 40 U/mL or higher, the proportion of patients with a 50% or greater decrease from baseline was measured.[17]

All toxicities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. The trial monitoring included 2 interim safety evaluations before the completion of accrual.

Statistical Analysis

In this 2-stage design, the first-stage analysis required that 21 of the first 35 evaluable patients be alive and progression free at 6 months to continue accrual. At completion, the trial required more than 43 of 67 evaluable patients to be alive and progression free at 6 months to conclude that the 6-month PFS rate was at least 70% (vs a null hypothesis of 55%) based on historical data from the Advanced Biliary Cancer (ABC)-02 and BINGO (Gemcitabine and Oxaliplatin With or Without Cetuximab in Advanced Biliary-Tract Cancer) trials.[2,4] This design had a 20% chance of falsely identifying the therapy as statistically nonsignificant if the true treatment success rate was 70% and a 5% chance of falsely concluding the therapy as significant if the true success rate was 55%. There was greater than 0.66 probability that the study would terminate at the first stage if the null hypothesis was true.

Distributions of PFS, TTP, and OS were estimated using the Kaplan-Meier approach (with pointwise confidence intervals for time-to-event outcomes), and univariate testing was performed using the log-rank test. Descriptive statistics were used for all clinical demographic data. The ORR and the DCR were summarized by number and percentage, with associations evaluated via the Fisher exact test. The preplanned determination of the association between change in serum CA19-9 level and survival was evaluated using a Cox proportional hazards regression model and the log-rank test. Safety data summaries described the incidence of adverse events (including severity and association with drug or treatment) and grade 3 or 4 toxic effects. For the final analysis, the data cutoff date was December 15, 2017, and 19 patients who were alive were censored for the survival analysis. Statistical analyses were completed using SAS (SAS Institute Inc), version 9.3. A 2-sided $P < .05$ was considered statistically significant.

Results

Patients

Seventy-four patients were enrolled at 23 community and academic centers across the United States and Europe between September 2014 and March 2016. The baseline demographic and disease characteristics of the patients are summarized in **Table 1**. The median age of the participants was 62 (range, 36-87) years and included 44 women (60%) and 68 white individuals (92%). Sixty-one patients (82%) had intrahepatic CCA. The patients received a median of 6 (range, 1-18) treatment cycles, and the median follow-up was 10.2 (range, 0.6-27.3) months.

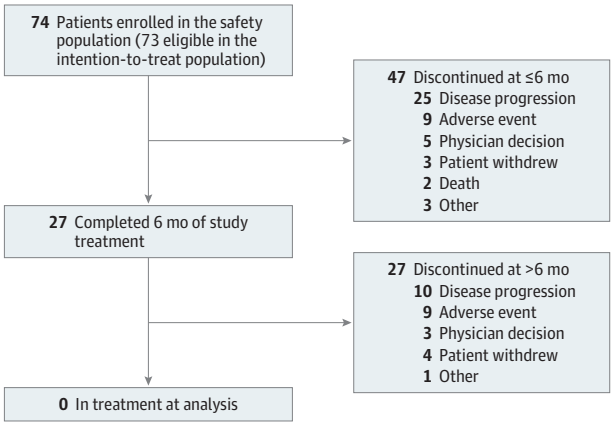
Patient disposition is summarized in **Figure 1**. Of the 73 patients in the intention-to-treat population (who received ≥1 dose of study treatment and were eligible for efficacy assessments), 47 (64%) discontinued treatment within 6 months of study initiation (25 [34%] discontinued due to progression), and 27 (36%) discontinued after 6 months (10 [14%] discontinued due to progression). In the stage 1 analysis, 19 of 35 patients were alive and progression free at 6 months, providing an observed 6-month PFS of 54%, which did not favor the alternative hypothesis. The trial was not halted, however, because the patient accrual for stage 2 had already been completed.

Table 1. Patient Baseline Demographic and Disease Characteristics (Safety Population)

Characteristic	Result
Total No. of patients progression free	74
Age, median (range), y	62 (36-87)
Female, No. (%)	44 (60)
Race, No. (%)	
White	68 (92)
African American	3 (4)
Asian	1 (1)
Other	2 (3)
Ethnicity, No. (%)	
Hispanic	1 (1)
Not Hispanic	72 (97)
Not reported	1 (1)
Time since initial diagnosis, days	
Mean (SD)	114.2 (409.5)
Median (range)	22 (4-3146)
ECOG performance status, No. (%)	
0	33 (45)
1	41 (55)
Tumor location, No. (%)	
Intrahepatic	61 (82)
Extrahepatic, perihilar	4 (5)
Extrahepatic, distal	9 (12)
AJCC stage in 69 patients, No. (%)	
II	11 (16)
III	3 (4)
IV	55 (80)
CA19-9, median (range), U/mL	158 (1-380 670)

Abbreviations: AJCC, American Joint Committee on Cancer; CA19-9, carbohydrate antigen 19-9; ECOG, Eastern Cooperative Oncology Group.

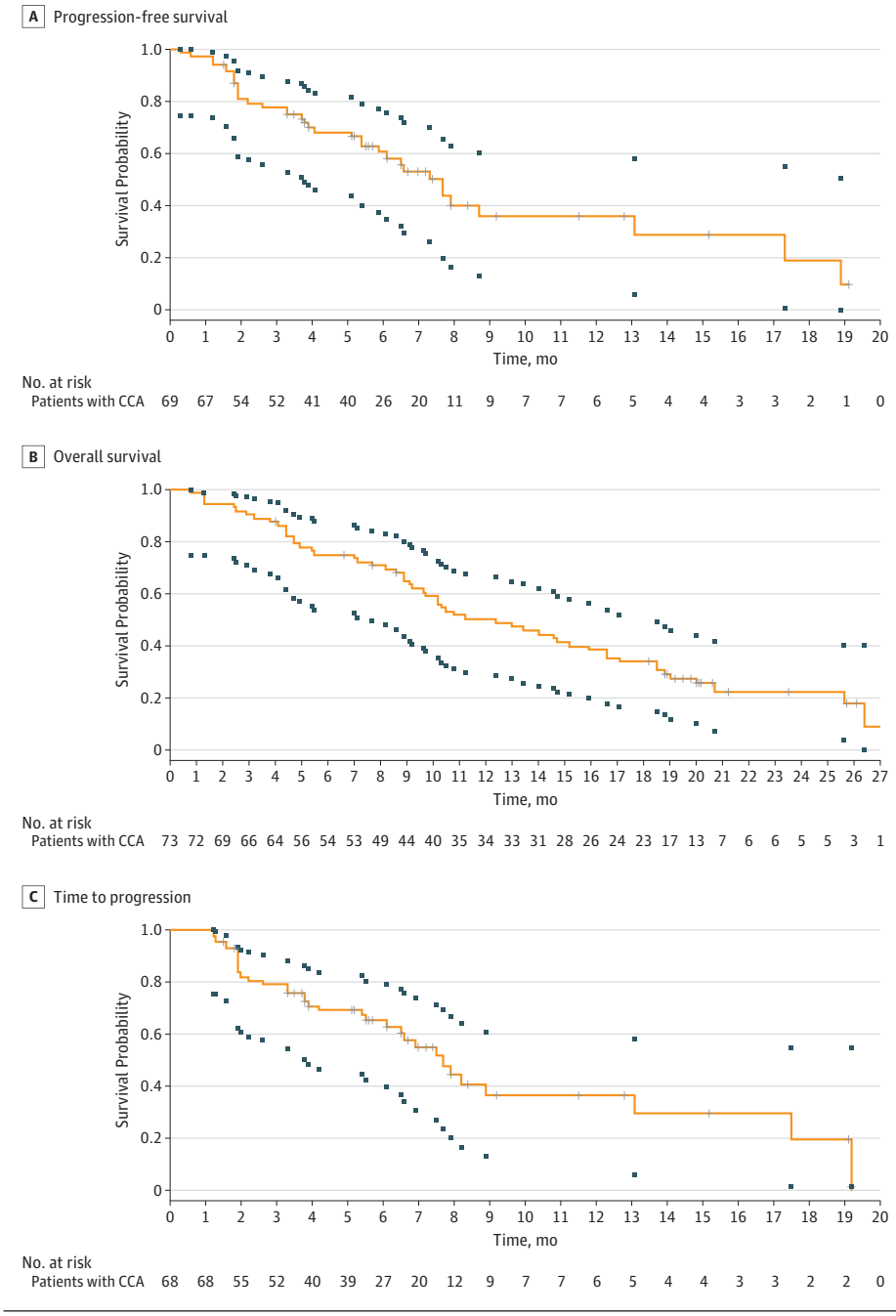
Figure 1. Patient Disposition



Efficacy Results

For the primary objective, the observed PFS rate at 6 months was 61% (95% CI, 48%-73%), which did not achieve the alternative hypothesis of 70%. It should be noted that the primary end point may be considered more descriptive because stage I analysis failed to reject the null hypothesis. The median PFS was 7.7 (95% CI, 5.4-13.1) months (**Figure 2**A), the median OS was 12.4 (95% CI, 9.2-15.9) months (Figure 2B), and the median TTP was

Figure 2. Kaplan-Meier Analyses of Survival Outcomes in the Intention-to-Treat Population



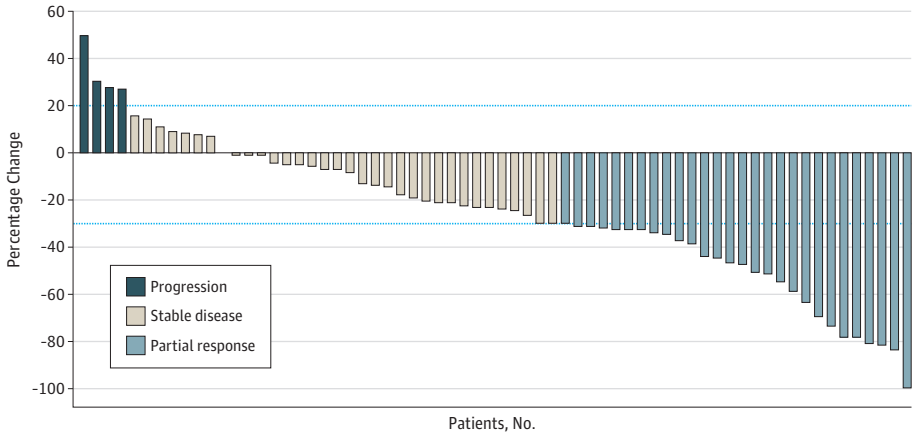
The boxes represent pointwise confidence intervals for time-to-event outcomes. Tick marks represent censored patients. Equal precision confidence intervals (small boxes) extend to the last event times. CCA indicates cholangiocarcinoma.

7.7 (95% CI, 6.1-13.1) months (Figure 2C). The confirmed best ORR and DCR were 30% and 66%, respectively (**Figure 3**). The hazard ratio for an association between the change in serum CA19-9 level and the median PFS as well as median OS were 2.02 (95% CI, 0.86-4.75) (P = .10) and 1.54 (95% CI, 0.64-3.71) (P = .34), respectively (eFigure in Supplement 2).

Safety

The study protocol permitted dose modifications but no change to the administration schedule for treatment-related adverse events. A total of 72 patients (97%) experienced a treatment-related adverse event (eTable in Supplement 2), the most common of which were fatigue (52 patients [70%]), neutropenia (50 patients [68%]), and peripheral neuropathy (41 patients [55%]). Overall, 61 patients (82%) experienced a grade 3 or higher treatment-related adverse event (**Table 2**). The most common treatment-related hematologic and nonhematologic adverse events at grade 3 or higher were neutropenia (32 patients [43%]) and fatigue (10 patients [14%]), respectively.

Figure 3. Waterfall Plot of Best Response per Response Evaluation Criteria in Solid Tumors, Version 1.1



Best overall response rate is 30% and disease control rate is 66%. The dashed line above the x-axis represents 20% increase in sum of target lesions from nadir, and the dashed line below the x-axis represents a 30% decrease in sum of target lesions from baseline.

Discussion

This single-arm, phase 2 multicenter trial evaluated the efficacy of the combination of nabP and gemcitabine treatment in patients with advanced or metastatic CCA. The PFS rate at 6 months was observed to be 61% in the intention-to-treat population and did not favor the alternative hypothesis. Nevertheless, the primary end point in this trial, along with the secondary efficacy end points of median PFS of 7.7 months and median OS of 12.4 months, was similar to that in the phase 3 ABC-02 trial (median PFS of 8.0 months and median OS of 11.7 months).[2] These data are also similar to those observed in the phase 2 gemcitabine plus oxaliplatin trial and gemcitabine plus capecitabine trials (median PFS of 6.1 and 6.2 months, and median OS of 12.4 and 12.7 months, respectively).[4,18] The present trial enrolled only patients with CCA, whereas the other mentioned trials also enrolled patients with gallbladder and ampullary cancers, which may have impacted the results. The observed best ORR of 30% in the present study is higher than that reported for patients with CCA in the gemcitabine plus oxaliplatin (20%) and gemcitabine plus cisplatin (19%) arms of the BINGO and ABC-02 trials, respectively.[2,4] The median follow-up time in the present trial was 10.2 months, with 19 patients alive at the time of data cutoff, and further follow-up may affect the overall survival estimate.

The combination treatment of nabP plus gemcitabine showed an acceptable safety profile among patients with CCA, and no new unexpected toxicities were observed in the present study. The most common treatment-related grade 3 or higher adverse events included neutropenia, thrombocytopenia, fatigue, and anemia and are consistent with those reported in the phase 3 Metastatic Pancreatic Adenocarcinoma Clinical Trial (MPACT), which evaluated gemcitabine plus nabP for treatment of pancreatic adenocarcinoma.[10] On the basis of the adverse event profile, nabP plus gemcitabine treatment may be considered for patients who are not otherwise considered candidates for cisplatin-based therapy, specifically those with renal dysfunction.

Table 2. Treatment-Related AEs at Grade 3 or Higher

Event	Patients, No. (%) (N = 74)
All hematologic AEs	
Neutropenia	32 (43)
Thrombocytopenia	12 (16)
Anemia	11 (15)
Leukopenia	7 (10)
Hemolytic uremic syndrome	3 (4)
Febrile neutropenia	2 (3)
Nonhematologic AEs in ≥5% of patients	
Fatigue	10 (14)
Elevated alkaline phosphatase level	7 (10)
Peripheral neuropathy	6 (8)
Diarrhea	5 (7)
Elevated alanine aminotransferase level	4 (5)
Hyponatremia	4 (5)

Abbreviation: AE, adverse event.

A recent phase 2, single-arm trial with liposomal paclitaxel plus gemcitabine treatment of 39 patients with unresectable or metastatic biliary cancers conducted in the Republic of Korea[19] reported a comparable median PFS and OS of 5.9 months and 11.9 months, respectively. The ORR was also comparable at 26%. It is unlikely that a randomized phase 2 or 3 clinical trial will be conducted with a noninferior statistical design. The addition of taxanes to gemcitabine, however, appears to be effective for treatment of CCA and is now being evaluated in combination with gemcitabine and cisplatin with encouraging preliminary data.[20]

Limitations

There are inherent limitations to the present trial, including the lack of a concurrent control arm and the small patient population. However, this multicenter study was conducted in both academic and community centers, which increases the generalizability of the data. The rate of enrollment was more

robust than anticipated for this rare cancer, enabling completion of accrual even before the stage 1 data could be analyzed.

Conclusions

In summary, treatment with nabP plus gemcitabine for patients with advanced CCA was found to have an acceptable safety profile. Although the trial did not meet its primary efficacy end point, the PFS and OS were comparable to those of the gemcitabine plus cisplatin and gemcitabine plus oxaliplatin regimens in the ABC-02 and BINGO trials, respectively.[2,4] As such, we conclude that combination nabP and gemcitabine therapy is well tolerated and may be considered as an alternative regimen to current therapeutic approaches in advanced CCA.

ARTICLE INFORMATION

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Author Contributions: Dr Sahai and Mr Catalano had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Sahai, Catalano, Nimeiri, Munshi, Benson, O'Dwyer.
Acquisition, analysis, or interpretation of data: Catalano, Zalupski, Lubner, Menge, Nimeiri, Munshi, Benson, O'Dwyer.
Drafting of the manuscript: Sahai, Catalano, Zalupski, Nimeiri, Benson, O'Dwyer.
Critical revision of the manuscript for important intellectual content: Sahai, Zalupski, Lubner, Menge, Nimeiri, Munshi, Benson, O'Dwyer.
Statistical analysis: Catalano.
Obtained funding: Sahai, Benson.
Administrative, technical, or material support: Sahai, Lubner, Nimeiri, Benson.
Supervision: Sahai, Lubner, Nimeiri, Munshi, Benson, O'Dwyer.

Conflict of Interest Disclosures: Dr Sahai reported serving as a paid consultant for Celgene, Halozyme, NewLink Genetics, and Incyte. Dr Benson reported serving as a paid consultant for Bristol-Myers Squibb, Guardant Health, Eli Lilly and Company, Exelixis, Purdue Pharma, Harborside Advisors, Xcenda AmerisourceBergen, National Comprehensive Cancer Network, Emron, inVentiv Health Inc, Axio, Genentech, Bayer, and Merck & Co. Dr O'Dwyer reported serving as a paid consultant for Boehringer Ingelheim, Genentech, and Celgene Corporation. No other disclosures were reported.

Funding/Support: Celgene Corporation provided the funding for this study.

Role of the Funder/Sponsor: Celgene Corporation reviewed and approved the manuscript but otherwise had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation of the manuscript; or the decision to submit the manuscript for publication.

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Completed

Phase II Trial of Nab-Paclitaxel and Gemcitabine for First-Line Treatment of Patients With Cholangiocarcinoma (**PrE0204**)

ClinicalTrials.gov ID NCT02181634

Sponsor PrECOG, LLC.

Information provided by PrECOG, LLC. (Responsible Party)

Last Update Posted 2018-10-03

Results Posted Tab

Results Overview

Conditions

Cholangiocarcinoma

Intervention/Treatment

- Drug: Nab-Paclitaxel and Gemcitabine

Other Study ID Numbers

- **PrE0204**
- AX-CL-OTHER-PrECOG-004080 (Other Grant/Funding Number) (OTHER_GRANT: Celgene)
- 2015-002066-24 (EudraCT Number)

Study Design

Allocation: N/A
Interventional Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Results Point of Contact

Name/Title: PrECOG Statistician
Organization: ECOG-ACRIN Biostatistics Center
Phone: 617-632-3633
Email: pcata@jimmy.harvard.edu

Enrollment (Actual)

74

Study Type

Interventional

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2014-07-02

First Posted (Estimated)
2014-07-04

Results Reporting Dates

Results First Submitted
2018-04-26

Results First Posted

2018-05-29

Study Record Updates

Last Update Posted

2018-10-03

Last Verified

2018-09

Participant Flow

Recruitment Details

[Not Specified]

Pre-assignment Details

[Not Specified]

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.

Period Title: **Overall Study**

Started	74
Eligible and Treated	73
Completed	2
Not Completed	72

Reason Not Completed

Lack of Efficacy	33
Adverse Event	17

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Physician Decision	8
Withdrawal by Subject	5
Death	2
Treatment delayed greater than 4 weeks	3
Ineligible	1
Max number of dose reduction	1
Symptomatic progression	1
Patient opted to proceed to surgery	1

Baseline Characteristics

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Baseline Participants	73
Baseline Analysis Population Description	Eligible and treated patients

Expand all / Collapse all

Age, Continuous

Median (Full Range) | Unit of measure: years

Number Analyzed	73 participants
	62 (36 to 87)

Sex: Female, Male

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	73 participants
Female	43 58.9%
Male	30 41.1%

Ethnicity (NIH/OMB)

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	73 participants
Hispanic or Latino	1 1.4%
Not Hispanic or Latino	71 97.3%

Unknown or Not Reported	1 1.4%

Race (NIH/OMB)

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	73 participants
American Indian or Alaska Native	0 0.0%
Asian	1 1.4%
Native Hawaiian or Other Pacific Islander	0 0.0%
Black or African American	3 4.1%
White	67 91.8%
More than one race	0 0.0%
Unknown or Not Reported	2 2.7%

Outcome Measures

Expand all / Collapse all

1. Progression-Free Survival (PFS) Rate at 6 Months (Proportion of Participants Alive and Progression-Free at 6 Months)

Type: Primary | Time Frame: Assessed at 6 months

Description	Progression-free survival is defined as the time from the date of first study treatment to either the date of documented disease progression or death from any cause, whichever occurred first. Progression-free survival rate at 6 months is defined as the proportion of patients who were disease progression-free and alive at 6 months. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), as a 20% increase in the sum of the diameter/axes of target lesions, taking as reference the smallest sum

	on study, or unequivocal progression of existing non-target lesions, or the appearance of new lesions.
Time Frame	Assessed at 6 months
Analysis Population Description	Eligible and treated
Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Measure Type: Number (95% Confidence Interval) | Unit of Measure: proportion of participants	0.605 (0.482 to 0.729)

2. Overall Survival (OS)

Type: Secondary | Time Frame: Every 3-6 months for up to 3 years

Description	OS is defined as the time from enrollment until death or last patient contact.
Time Frame	Every 3-6 months for up to 3 years
Analysis Population Description	Eligible and treated

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Median (95% Confidence Interval) | Unit of Measure: months	11.2 (9.6 to 14.7)

3. Progression-free Survival (PFS)

Type: Secondary | Time Frame: Every 3-6 months for up to 3 years

Description	Progression-free survival is defined as the time from the date of first study treatment to either the date of documented disease progression or death from any cause, whichever occurred first.
Time Frame	Every 3-6 months for up to 3 years
Analysis Population Description	Eligible and treated patients
Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Median (95% Confidence Interval) | Unit of Measure: months	7.7 (5.9 to 13.1)

4. Time To Progression (TTP)

Type: Secondary | Time Frame: Every 3-6 months for up to 3 years

Description	TTP was defined as the time from date of first dose of study therapy to date of removal from study for progression. Patients who have not experienced progression were censored at the date of last disease evaluation. Progression is evaluated using Solid Tumor Response Criteria (RECIST) Version 1.1. Progression is defined as at least a 20% increase in the sum of the diameters/axes of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5mm over the nadir. The appearance of new lesions or unequivocal progression of existing non-target lesions also constitutes disease progression.
Time Frame	Every 3-6 months for up to 3 years
Analysis Population Description	Eligible and treated
Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Median (95% Confidence Interval) | Unit of Measure: months	7.7 (6.5 to 13.1)

5. Overall Response Rate (ORR)

Type: Secondary | Time Frame: Every 3-6 months for up to 3 years

Description	Overall response rate is defined as the proportion of patients with complete response or partial response per RECIST version 1.1. Complete response is defined as disappearance of all lesions. Partial response is defined as at least a 30% decrease in the sum of the

	diameters/axes of target lesions and the persistence of one or more non-target lesion(s) and/or the maintenance of tumor marker levels above the normal limits. A confirmation assessment performed >=4 weeks after the criteria for response is met is required.
Time Frame	Every 3-6 months for up to 3 years
Analysis Population Description	Eligible and treated
Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Measure Type: Number (95% Confidence Interval) | Unit of Measure: proportion of participants	0.301 (0.199 to 0.420)

6. Disease Control Rate (DCR)

Type: Secondary | Time Frame: Every 3-6 months for up to 3 years

Description	Disease control rate is the proportion of patients achieved complete response, partial response or stable disease per RECIST version 1.1. Complete response is defined as disappearance of all lesions. Partial response is defined as at least a 30% decrease in the sum of the diameters/axes of target lesions and the persistence of one or more non-target lesion(s) and/or the maintenance of tumor marker levels above the normal limits. Stable disease is defined as neither sufficient shrinkage to qualify for complete or partial response nor sufficient increase to qualify for progression. A confirmation assessment performed >=4 weeks after the criteria for response is met is required.
Time Frame	Every 3-6 months for up to 3 years

Analysis Population Description	Eligible and treated patients
Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	73
Measure Type: Number (95% Confidence Interval) | Unit of Measure: proportion of participants	0.658 (0.537 to 0.765)

7. Association Between PFS and Maximum Change in Carbohydrate Antigen (CA) 19-9 From Baseline

Type: Secondary | Time Frame: CA 19-9 was evaluated every 8 weeks until progression or for up to 3 years and off-treatment

Description	Patients were dichotomized into maximum CA 19-9 decline >=50% and maximum CA 19-9 decline <50%. Cox proportional hazards model was used to evaluate the association between PFS and maximum change in CA 19-9.
Time Frame	CA 19-9 was evaluated every 8 weeks until progression or for up to 3 years and off-treatment
Analysis Population Description	Eligible and treated patients with CA 19-9 data available

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	35

CA 19-9 decline >=50%

Number Analyzed	26 participants
∗Median (95% Confidence Interval) | Unit of Measure: months	7.7 (6.6 to 13.1)

OS and Maximum Change in Carbohydrate Antigen (CA) 19-9

CA 19-9 decline <50%

Number Analyzed	9 participants
*	1.9 (1.6 to 18.2)

Frame: CA 19-9 was evaluated every 8 weeks until progression or f-treatment

Patients were dichotomized into maximum CA 19-9 decline >=50% and maximum CA 19-9 decline <50%. Cox proportional hazards model was used to evaluate the association between OS and maximum change in CA 19-9.

* Median (95% Confidence Interval) | Unit of Measure: months

Time Frame	CA 19-9 was evaluated every 8 weeks until progression or for up to 3 years and off-treatment
Analysis Population Description	Eligible and treated patients with CA 19-9 data available

Statistical Analysis 1 : Nab-Paclitaxel and Gemcitabine | Superiority | Log-Rank

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Overall Number of Participants Analyzed	35

CA 19-9 decline >=50%

Number Analyzed	26 participants
*Median (95% Confidence Interval) | Unit of Measure: months	14.6 (10.2 to 25.6)

Tumor Cells (CTCs)

d | Time Frame: Prior to Cycle 1, Day 1; Cycle 1 Day 8; Cycle 3, Day

CA 19-9 decline <50%

Number Analyzed	9 participants
*	10.2 [1] (4.1 to NA)

Correlate change in CTCs to median PFS, OS, TTP, ORR and DCR.

Prior to Cycle 1, Day 1; Cycle 1 Day 8; Cycle 3, Day 1 and at Off Treatment

* Median (95% Confidence Interval) | Unit of Measure: months

[Not Specified]

[1] The upper limit of the 95% confidence interval was not calculable because an insufficient number of participants reached the event at the final time point for assessment.

ita Not Reported

ression

d | Time Frame: Baseline

Description	Correlate stromal SPARC (high versus low) expression by immunohistochemistry (IHC) with median PFS, OS, TTP, ORR and DCR.
Time Frame	Baseline
Analysis Population Description	[Not Specified]

Statistical Analysis 1 : Nab-Paclitaxel and Gemcitabine | Superiority | Log Rank

Outcome Measure Data Not Reported

11. Fibrosis Expression

Type: Other Pre-specified | Time Frame: Baseline

Description	Correlate fibrosis (low, intermediate and high) by trichrome staining with median PFS, OS, TTP, ORR and DCR.
Time Frame	Baseline
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

12. CDA Expression

Type: Other Pre-specified | Time Frame: Baseline

Description	Correlate CDA (high versus low) expression by IHC with median PFS, OS, TTP, ORR and DCR.
Time Frame	Baseline
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

13. hENT Expression

Type: Other Pre-specified | Time Frame: Baseline

Description	Correlate hENT1 (high versus low) expression by IHC with median PFS, OS, TTP, ORR and DCR.
Time Frame	Baseline
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

14. Banking Biospecimens for Future Assessment

Type: Other Pre-specified | Time Frame: Prior to Cycle 1, Day 1; Cycle 1, Day 8; Cycle 3, Day 1 and at Off Treatment

Description	Optional specimen banking of patient blood specimens (including serum, plasma and buffy coat) as well as fixed left-over tissue specimens when available from all enrolled patients in this trial for

	possible future molecular, pharmacogenomic, and/or proteomic testing.
Time Frame	Prior to Cycle 1, Day 1; Cycle 1, Day 8; Cycle 3, Day 1 and at Off Treatment
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

Adverse Events

Time Frame
Assessed every week for the first 2 cycles, then every two cycles (every 8 weeks) and 30 days after the last dose of therapy

Adverse Event Reporting Description
[Not Specified]

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.

All-Cause Mortality

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
	Affected / at Risk (%)
Total	–/--

Serious Adverse Events

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
	Affected / at Risk (%)
Total	42/74 (56.76%)
Blood and lymphatic system disorders	
Anemia †1	1/74 (1.35%)
Febrile neutropenia †1	2/74 (2.70%)
Haemolytic uraemic syndrome †1	3/74 (4.05%)
Neutropenia †1	1/74 (1.35%)
Cardiac disorders	
Atrial fibrillation †1	2/74 (2.70%)
Cardiac failure †1	1/74 (1.35%)
Cardiac failure congestive †1	1/74 (1.35%)
Pericardial effusion †1	1/74 (1.35%)
Tachycardia †1	1/74 (1.35%)
Gastrointestinal disorders	
Abdominal pain †1	3/74 (4.05%)
Ascites †1	2/74 (2.70%)
Constipation †1	1/74 (1.35%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Diarrhea †1	3/74 (4.05%)
Gastrointestinal haemorrhage †1	1/74 (1.35%)
General disorders	
Disease progression †1	2/74 (2.70%)
Fatigue †1	1/74 (1.35%)
Generalised oedema †1	2/74 (2.70%)
Multi-organ failure †1	2/74 (2.70%)
Oedema peripheral †1	1/74 (1.35%)
Pyrexia †1	5/74 (6.76%)
Hepatobiliary disorders	
Bile duct obstruction †1	1/74 (1.35%)
Bile duct stenosis †1	2/74 (2.70%)
Biliary fistula †1	1/74 (1.35%)
Cholangitis †1	3/74 (4.05%)
Cholecystitis †1	1/74 (1.35%)
Cholestasis †1	1/74 (1.35%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Hyperbilirubinaemia †1	3/74 (4.05%)

Infections and infestations

Abscess †1	1/74 (1.35%)
Biliary tract infection †1	1/74 (1.35%)
Clostridium difficile infection †1	1/74 (1.35%)
Device related infection †1	2/74 (2.70%)
Diverticulitis †1	1/74 (1.35%)
Emphysematous cholecystitis †1	1/74 (1.35%)
Infection †1	1/74 (1.35%)
Lung infection †1	1/74 (1.35%)
Neutropenic sepsis †1	1/74 (1.35%)
Pneumonia †1	1/74 (1.35%)
Sepsis †1	4/74 (5.41%)

Injury, poisoning and procedural complications

Humerus fracture †1	1/74 (1.35%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Post procedural haemorrhage †1	1/74 (1.35%)
Investigations	
Neutrophil count decreased †1	1/74 (1.35%)
Metabolism and nutrition disorders	
Hyponatraemia †1	1/74 (1.35%)
Hypovolaemia †1	1/74 (1.35%)
Nervous system disorders	
Encephalopathy †1	1/74 (1.35%)
Facial nerve disorder †1	1/74 (1.35%)
Haemorrhage intracranial †1	1/74 (1.35%)
Headache †1	1/74 (1.35%)
Hepatic encephalopathy †1	1/74 (1.35%)
Syncope †1	1/74 (1.35%)
Renal and urinary disorders	
Acute kidney injury †1	2/74 (2.70%)
Renal failure †1	1/74 (1.35%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.

Acute respiratory distress syndrome †1	1/74 (1.35%)
Dyspnoea †1	1/74 (1.35%)
Pneumonitis †1	1/74 (1.35%)
Pulmonary embolism †1	1/74 (1.35%)
Respiratory failure †1	2/74 (2.70%)

Skin and subcutaneous tissue disorders

Rash macular †1	1/74 (1.35%)
Rash maculo-papular †1	1/74 (1.35%)

Vascular disorders

Deep vein thrombosis †1	3/74 (4.05%)
Embolism †1	3/74 (4.05%)
Hypertension †1	1/74 (1.35%)
Hypotension †1	1/74 (1.35%)
Thrombosis †1	1/74 (1.35%)

† Indicates events were collected by

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
	Affected / at Risk (%)
Total	72/74 (97.30%)
Blood and lymphatic system disorders	
Anemia †1	31/74 (41.89%)
Neutropenia †1	26/74 (35.14%)
Eye disorders	
Vision blurred †1	5/74 (6.76%)
Gastrointestinal disorders	
Abdominal distension †1	5/74 (6.76%)
Abdominal pain †1	12/74 (16.22%)
Ascites †1	5/74 (6.76%)
Constipation †1	34/74 (45.95%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Decreased appetite †1	28/74 (37.84%)
Diarrhea †1	35/74 (47.30%)
Dry mouth †1	4/74 (5.41%)
Nausea †1	34/74 (45.95%)
Stomatitis †1	8/74 (10.81%)
Vomiting †1	18/74 (24.32%)

General disorders

Asthenia †1	5/74 (6.76%)
Chills †1	11/74 (14.86%)
Fatigue †1	53/74 (71.62%)
Influenza like illness †1	4/74 (5.41%)
Oedema peripheral †1	31/74 (41.89%)
Pain †1	7/74 (9.46%)
Pyrexia †1	18/74 (24.32%)

Infections and infestations

Mucosal inflammation †1	4/74 (5.41%)
Sepsis †1	4/74 (5.41%)

Investigations

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Alanine aminotransferase increased [†1]	18/74 (24.32%)
Aspartate aminotransferase increased [†1]	18/74 (24.32%)
Blood alkaline phosphatase increased [†1]	17/74 (22.97%)
Blood bilirubin increased [†1]	7/74 (9.46%)
Hyperbilirubinemia [†1]	7/74 (9.46%)
Hypoalbuminemia [†1]	9/74 (12.16%)
Hypocalcemia [†1]	4/74 (5.41%)
Leukopenia [†1]	5/74 (6.76%)
Neutrophil count decreased [†1]	14/74 (18.92%)
Platelet count decreased [†1]	11/74 (14.86%)
Thrombocytopenia [†1]	16/74 (21.62%)
Weight decreased [†1]	22/74 (29.73%)
Weight increased [†1]	5/74 (6.76%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
White blood cell count decreased †1	10/74 (13.51%)

Metabolism and nutrition disorders

Dehydration †1	7/74 (9.46%)
Hypokalaemia †1	7/74 (9.46%)
Hyponatremia †1	8/74 (10.81%)

Musculoskeletal and connective tissue disorders

Arthralgia †1	13/74 (17.57%)
Back pain †1	6/74 (8.11%)
Bone pain †1	4/74 (5.41%)
Muscular weakness †1	14/74 (18.92%)
Musculoskeletal pain †1	5/74 (6.76%)
Myalgia †1	8/74 (10.81%)
Pain in extremity †1	9/74 (12.16%)

Nervous system disorders

Dizziness †1	11/74 (14.86%)
Dysgeusia †1	17/74 (22.97%)
Headache †1	6/74 (8.11%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Neuropathy peripheral †1	28/74 (37.84%)
Peripheral sensory neuropathy †1	9/74 (12.16%)
Tremor †1	4/74 (5.41%)
Psychiatric disorders	
Insomnia †1	12/74 (16.22%)
Renal and urinary disorders	
Acute kidney injury †1	5/74 (6.76%)
Respiratory, thoracic and mediastinal disorders	
Cough †1	11/74 (14.86%)
Dyspnea †1	22/74 (29.73%)
Epistaxis †1	11/74 (14.86%)
Pleural effusion †1	4/74 (5.41%)
Skin and subcutaneous tissue disorders	
Alopecia †1	39/74 (52.70%)
Nail discolouration †1	5/74 (6.76%)
Pruritus †1	5/74 (6.76%)
Rash †1	9/74 (12.16%)

Arm/Group Title	Nab-Paclitaxel and Gemcitabine
Arm/Group Description	Nab-Paclitaxel 125 mg/m² IV and Gemcitabine 1000 mg/m² on days 1, 8 and 15 every 28 days until progression or unacceptable toxicity. Nab-Paclitaxel and Gemcitabine: Nab-Paclitaxel will be administered first, at a dose of 125 mg/m² IV over a period of 30 minutes; gemcitabine will be administered second, at a dose of 1000 mg/m² over a period of 30 minutes.
Rash maculo-papular †1	7/74 (9.46%)

Vascular disorders

Deep vein thrombosis †1	5/74 (6.76%)
Embolism †1	4/74 (5.41%)
Hot flashes †1	6/74 (8.11%)
Hypertension †1	10/74 (13.51%)

† Indicates events were collected by systematic assessment

1 Term from vocabulary, CTCAE (4.0)

Limitations and Caveats

[Not Specified]

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

PrECOG, LLC.

Collaborators

- Celgene Corporation

Investigators

- Study Chair: Vaibhav Sahai, MD, University of Michigan Health System in Ann Arbor, MI

Publications

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- Sahai V, Catalano PJ, Zalupski MM, Lubner SJ, Menge MR, Nimeiri HS, Munshi HG, Benson AB 3rd, O'Dwyer PJ. Nab-Paclitaxel and Gemcitabine as First-line Treatment of Advanced or Metastatic Cholangiocarcinoma: A Phase 2 Clinical Trial. JAMA Oncol. 2018 Dec 1;4(12):1707-1712. doi: 10.1001/jamaoncol.2018.3277. (https://pubmed.ncbi.nlm.nih.gov/30178032)

More Information

Record History

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed