

Научно-технические проекты

- «Разработать и внедрить метод лечения пациентов, страдающих раком поджелудочной железы, при помощи аутологичных дендритных клеток» подпрограммы «Трансплантация клеток, тканей и органов» (сокращенное наименование подпрограммы) государственной научно-технической программы «Новые методы оказания медицинской помощи» 2016-2020 годы

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ



МЕТОД ПРОГНОЗИРОВАНИЯ ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ЗЛОКАЧЕСТВЕННЫХ НОВООБРАЗОВАНИЙ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ

инструкция по применению

УЧРЕЖДЕНИЯ - РАЗРАБОТЧИКИ:

Государственное учреждение «Республиканский научно-практический центр эпидемиологии и микробиологии»

Учреждение образования «Белорусский государственный медицинский университет»

Учреждение здравоохранения «Минский городской клинический онкологический диспансер»

АВТОРЫ: канд. мед. наук Гончаров А.Е., д-р. мед. наук, проф. Прохоров А.В., Бушик О.В., Романовская С.Э., Колошко Л.Р.

Минск, 2018

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ



МЕТОД ЛЕЧЕНИЯ ПАЦИЕНТОВ, СТРАДАЮЩИХ РАКОМ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ, С ПРИМЕНЕНИЕМ МОНОЦИТАРНЫХ ДЕНДРИТНЫХ КЛЕТОК

инструкция по применению

УЧРЕЖДЕНИЯ - РАЗРАБОТЧИКИ:

Государственное учреждение «Республиканский научно-практический центр эпидемиологии и микробиологии», учреждение образования «Белорусский государственный медицинский университет», учреждение здравоохранения «Минский городской клинический онкологический диспансер»

АВТОРЫ: канд. мед. наук Гончаров А.Е., д-р. мед. наук, проф. Прохоров А.В., Тимохина О.В., Романовская С.Э., Дуж Е.В., Бобрукевич Д.В., Романова И.В., канд. биол. наук Антоневич Н.Г., Рында Е.Г.

Минск, 2019

Акты внедрения

- [Акт внедрения 1](#)
- [Акт внедрения 2](#)
- [Акт внедрения МГКОД](#)
- [Акт внедрения БелМапо](#)
- [Акт внедрения БГМУ](#)
- [Акт внедрения ЦОКи 2021 ИБиКИ](#)
- [Акт РПЖ июнь 2021 ИБКИ](#)

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2. Andrei Y.Hancharou, O.Buschik, A.Prokhorov, S.Romanovskaya, Lawrence M.Dubuske Expression of B7-Family Co-inhibitory Molecules by Dendritic Cells from Pancreatic Cancer Patients. Journal of Allergy and Clinical Immunology. Vol. 143, Issue 2, Supplement, February 2019, Page AB18
3. Hancharou A, Timohina O, Prokhorov A, Romanovskaya S, Dubuske LM. Minor leukocyte subsets in patients with stage Ii pancreatic cancer. Allergy. Abstracts from the European Academy of Allergy and Clinical Immunology Congress 01–05 June 2019 Lisbon, Portugal. P465, TP0824
4. Гончаров А.Е., Прохоров А.В., Тимохина О.В. Применение дендритных клеток в комплексном лечении рака поджелудочной железы. Гены и Клетки. 2019. Т. 14. № 5. С. 66.
5. Прохоров А.В. Клеточная иммунотерапия в комплексном лечении рака поджелудочной железы. Злокачественные опухоли. 2019.Т: 9: 3S1, С. 69
6. Прохоров А.В., Гончаров А.Е., Тур Г.Е., Романовская С.Э., Тимохина О.В. Клеточная иммунотерапия в комплексном лечении рака поджелудочной железы. В сборнике: Хирургия Беларуси на современном этапе. материалы XVI съезда хирургов Республики Беларусь и Республиканской научно-практической конференции: в 2 частях. 2018. С. 44-46.

- «Разработать и внедрить метод метрономной поддерживающей химиотерапии пациентов с диссеминированным колоректальным раком» подпрограммы «Онкологические заболевания» ГНТП «Новые методы оказания медицинской помощи» 2016- 2022 гг.

Защита диссертации (2021 г.)

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Министерство здравоохранения Республики Беларусь



Заместитель министра

Д.Л. Пиневиц

июня 2019 г.

Регистрационный № 085-0619

МЕТОД МЕТРОНОМНОЙ ПОДДЕРЖИВАЮЩЕЙ ХИМИОТЕРАПИИ КОЛОРЕКТАЛЬНОГО РАКА

Инструкция по применению

Учреждение–разработчик: государственное учреждение
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к.м.н. Субоч Е.И., д.м.н., проф. Прохоров А.В., д.м.н. Портянко А.С.

Акты внедрения

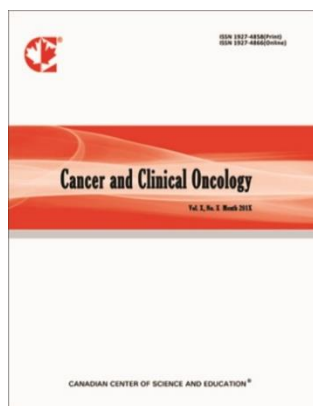
- [Акт внедрения МГКОЦ](#)

Публикации



Стрельцова О.В., Прохоров А.В. Метрономная химиотерапия в лечении онкологических заболеваний// Медицинский журнал №2 (64)-2018. С.89-94.

Алехнович В.Ю., Прохоров А.В. Сравнительный анализ комплексного лечения метастатического колоректального рака// Медицинский журнал №2 (64)-2018. С.21-26



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Maintenance Metronomic Chemotherapy in Treatment of Metastatic Colorectal Cancer

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Abstract

Treatment of metastatic colorectal cancer (mCRC) is one of the most challenging and important problems in oncology at present moment. This article presents the interim results of treatment of patients with colorectal cancer, who were enrolled from 2016 till 2019 (n=60) with the use of maintenance metronomic chemotherapy. Metronomic regimen consisted of oral capecitabine 500 mg 3 times a day and oral cyclophosphane 50 mg daily. The control arm consisted of mCRC patients who received the same induction chemotherapy without maintenance from 2011 till 2015 (n=70). Median follow-up time was 18.5 months. Median progression-free survival (PFS) was 9.0 and 7.4 months in the maintenance and control arms respectively. Median overall survival (OS), counted from the beginning of induction chemotherapy, is currently 22.9 months in the maintenance arm, and 14.7 months in control. High expression levels of genes, encoding enzymes TS (thymidylate synthetase), DPD (dihydropyrimidine dehydrogenase) and receptor VEGFR1, low expression level of gene TP (thymidylate phosphorylase), as well as low levels of tumor markers CEA and CA 19-9 are the prognostic factors of sensitivity to metronomic chemotherapy given to colorectal cancer patients. Based on these data, we identified a group of patients who are recommended to use this method of treatment.

Keywords: metronomic chemotherapy, angiogenesis, survival rates, colorectal cancer, maintenance therapy



Стрельцова О.В., Прохоров А.В. Метрономная химиотерапия в лечении онкологических заболеваний. Онкологический журнал. 2018. Т. 12. № 1 (45). С. 89-94



Стрельцова О.В., Прохоров А.В., Баранов Е.В. Метрономная поддерживающая химиотерапия в лечении диссеминированного колоректального рака// X съезд онкологов и радиологов стран СНГ и Евразии 23-25 апреля 2018, Сочи, Россия Евразийский онкологический журнал. 2018, т.6, №1 с.415



Алехнович В.Ю., Прохоров А.В. Радиочастотная абляция в лечении метастазов колоректального рака в печень. Медицина, 2015 4(91): 26-29

- «Разработать биомедицинский клеточный продукт на основе моноцитарных дендритных клеток для лечения и медицинской профилактики рецидивного рака мочевого пузыря» подпрограммы 1 «Инновационные биотехнологии – 2020» Государственной программы «Научные технологии и техника» на 2016 – 2020 годы

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
РЕСПУБЛИКИ БЕЛАРУСЬ



**МЕТОД ЛЕЧЕНИЯ ПАЦИЕНТОВ, СТРАДАЮЩИХ РЕЦИДИВОМ
МЫШЕЧНО-НЕИНВАЗИВНОГО РАКА МОЧЕВОГО ПУЗЫРЯ,
С ПРИМЕНЕНИЕМ БИОМЕДИЦИНСКОГО КЛЕТОЧНОГО
ПРОДУКТА НА ОСНОВЕ АУТОЛОГИЧНЫХ ДЕНДРИТНЫХ
КЛЕТОК**

инструкция по применению

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АВТОРЫ: канд. мед. наук, доц. Гончаров А.Е., д-р. мед. наук, проф. Прохоров А.В., канд. биол. наук Антонович Н.Г., Тимохина О.В., Прохоров В.А.

Минск, 2020

Акты внедрения

- [Акт внедрения в ИБКИ \(ДК-РМП\) 2022\[8838\]](#)

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- Прохоров В.А., Гончаров А.Е., Антоневиц Н.Г., Масанский И.Л. Клеточная иммунотерапия в комплексном лечении немышечно-инвазивного рака мочевого пузыря на основе аутологичных дендритных клеток// Современные технологии в медицинском образовании [Электронный ресурс] : материалы международной научно-практической конференции, посвященной 100-летию Белорус. гос. мед. ун-та, Республика Беларусь, г. Минск, 1-5 ноября 2021 г. / под ред. С.П. Рубниковича, В.А. Филонюка. – Минск : БГМУ, 2021-с.436-439

«Клиническое применение методов определения иммунофенотипического профиля циркулирующих опухолевых клеток и циркулирующих раковых стволовых клеток в диагностике и лечении злокачественных новообразований основных локализаций» по мероприятию 52 «Разработать методы определения иммунофенотипического профиля циркулирующих опухолевых клеток и циркулирующих раковых стволовых клеток» подпрограммы 1 «Инновационные биотехнологии – 2020» Государственной программы «Наукоемкие технологии и техника» на 2016 – 2020 годы.



МЕТОД ОПРЕДЕЛЕНИЯ СОДЕРЖАНИЯ ЦИРКУЛИРУЮЩИХ
РАКОВЫХ СТЕЛОВЫХ КЛЕТОК В ПЕРИФЕРИЧЕСКОЙ КРОВИ
У ПАЦИЕНТОВ, СТРАДАЮЩИХ ЗЛОКАЧЕСТВЕННЫМИ
НОВООБРАЗОВАНИЯМИ ЭПИТЕЛИАЛЬНОЙ ПРИРОДЫ
инструкция по применению

УЧРЕЖДЕНИЯ-РАЗРАБОТЧИКИ: государственное научное учреждение «Институт биофизики и клеточной инженерии НАН Беларуси», учреждение образования «Белорусский государственный медицинский университет»

АВТОРЫ: канд. биол. наук Дмитрук О.Г., Абашкин В.М., канд. мед. наук, доц. Гончаров А.Е., д-р. мед. наук, проф. Прохоров А.В., канд. мед. наук Тур Г.Е., д-р биол. наук, доц. Щербин Д.Г., канд. мед. наук, доц. Колобухов А.Э.

Минск, 2020

Акты внедрения

- [Акт внедрения цРСК 191.2-1220 2021 МГКОД](#)
- [Акт внедрения ЦОК 191.1-1220 2021 МГКОД](#)

Публикации



Позняк Т.А., Гончаров А.Е., Абашкин В.М., Становая А.И., Прохоров А.В., Щербин Д.Г. Циркулирующие опухолевые клетки и циркулирующие раковые стволовые клетки и их детекция методом проточной цитофлуориметрии. Весті Нацыянальнай Акадэміі Навук Беларусі. Серыя біялагічных навук. 2021, Том: 66: 3, с. 370-384

В обзоре приведено описание циркулирующих раковых стволовых клеток (цРСК) и циркулирующих опухолевых клеток (ЦОК) в крови человека и методов их определения. цРСК являются одними из главных инициаторов рецидива онкологических заболеваний, что делает их основной мишенью для разработки новых методов лечения. ЦОК являются относительно новыми биомаркерами для ранней диагностики метастазирования, мониторинг содержания которых дает ценную информацию на всех этапах ведения онкопациентов, включая раннюю диагностику заболевания, оценку риска

рецидива болезни, определение эффективности химиотерапии с возможностью последующей ее коррекции.

- Гончаров А.Е., Тимохина О.В., Прохоров А.В., Романовская С.Э., Колошко Л.Р. Детекция циркулирующих опухолевых клеток у пациентов со злокачественными новообразованиями органов брюшной полости. Современные проблемы инфекционной патологии человека ГУ «РНПЦ эпидемиологии и микробиологии». Сборник научных трудов. Выпуск 11, Минск 2018. с.154-158

«Клиническое применение и оценка эффективности биомедицинского клеточного продукта на основе цитокин-индуцированных киллерных клеток в лечении рецидивной и метастатической уротелиальной карциномы» по мероприятию «Разработать биомедицинский клеточный продукт на основе цитокин-индуцированных киллерных клеток» подпрограммы «Инновационные биотехнологии – 2025» Государственной программы «Наукоёмкие технологии и техника» на 2021–2025 годы

Гончаров А.Е., Прохоров А.В., Тимохина О.В., Антоневиц Н.Г., Минич Я.С., Рында Е.Г., Прохоров В.А. Применение биомедицинского клеточного продукта на основе моноцитарных дендритных клеток в лечении пациентов, страдающих раком мочевого пузыря: результаты клинического исследования. В сборнике: БГМУ в авангарде медицинской науки и практики. рецензируемый ежегодный сборник научных трудов. Министерство здравоохранения Республики Беларусь; Белорусский государственный медицинский университет. Минск, 2021. С. 205-215.

Международные клинические испытания

- Randomized, Double-Blind, Phase 3 Study Evaluating TAS-102 Plus Best Supportive Care (BSC) Versus Placebo Plus BSC In Patients With Metastatic Gastric Cancer Refractory to Standard Treatments (TAGS)

THE LANCET
Oncology

Kohei Shitara, Toshihiko Doi, Mikhail Dvorkin, Wasat Mansoor, Hendrik-Tobias Arkenau, Aliaksandr Prokharau et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol.2018 Nov;19(11):1437-1448

Abstract

Background: Trifluridine/tipiracil showed activity and was well tolerated in a phase 2 study of pretreated patients with advanced gastric cancer done in Japan. We investigated whether the treatment was efficacious compared with placebo in a global population.

Methods: TAGS was a randomised, double-blind, placebo-controlled, phase 3 trial done in 110 academic hospitals in 17 countries. Patients aged 18 years or older with histologically confirmed, non-resectable, metastatic gastric adenocarcinoma (including adenocarcinoma of the gastroesophageal junction) as defined by the American Joint Committee on Cancer staging classification (7th edition) who had received at least two previous chemotherapy regimens and had experienced radiological disease progression were eligible for inclusion. Patients were randomly assigned (2:1) via dynamic randomisation from a centralised interactive voice-response system to receive either oral trifluridine/tipiracil (35 mg/m² twice daily on days 1-5 and days 8-12 every 28 days) plus best supportive care or placebo plus best supportive care. Participants were allocated to groups by study-site personnel. Randomisation was stratified by region (Japan vs rest of world), ECOG performance status (0 vs 1), and previous treatment with ramucirumab (yes vs no). Both patients and investigators were masked to treatment allocation. The primary endpoint was overall survival. Efficacy was assessed in the intention-to-treat population and safety in all patients who received at least one dose of treatment. This trial is registered with ClinicalTrials.gov, number NCT02500043. The trial, including follow-up of all participants, has been completed.

Findings: Between Feb 24, 2016, and Jan 5, 2018, 507 patients were enrolled and randomly assigned, 337 to the trifluridine/tipiracil group and 170 to the placebo group. Median overall survival was 5·7 months (95% CI 4·8-6·2) in the trifluridine/tipiracil group and 3·6 months (3·1-4·1) in the placebo group (hazard ratio 0·69 [95% CI 0·56-0·85]; one-sided $p=0·00029$, two-sided $p=0·00058$). Grade 3 or worse adverse events of any cause occurred in 267 (80%) patients in the trifluridine/tipiracil group and 97 (58%) in the placebo group. The most frequent grade 3 or worse adverse events of any cause were neutropenia ($n=114$ [34%]) and anaemia ($n=64$ [19%]) in the trifluridine/tipiracil group and abdominal pain ($n=15$ [9%]) and general deterioration of physical health ($n=15$ [9%]) in the placebo group. Serious adverse events of any cause were reported in 143 (43%) patients in the trifluridine/tipiracil group and 70 (42%) in the placebo group. One treatment-

related death was reported in each group (because of cardiopulmonary arrest in the trifluridine/tipiracil group and because of toxic hepatitis in the placebo group).

Interpretation: Trifluridine/tipiracil significantly improved overall survival compared with placebo and was well tolerated in this heavily pretreated population of patients with advanced gastric cancer. Trifluridine/tipiracil could be a new treatment option in this population who represent a high unmet medical need.

JAMA Oncology

David H. Ilson, Josep Tabernero, Aliaksandr Prokharau et al.
Efficacy and Safety of Trifluridine/Tipiracil Treatment in Patients With Metastatic Gastric Cancer Who Had Undergone Gastrectomy. Subgroup Analyses of a Randomized Clinical Trial. *JAMA Oncol.* 2020 Jan; 6(1): e193531.

Abstract

Importance: Trifluridine/tipiracil (FTD/TPI) treatment has shown clinical benefit in patients with pretreated metastatic gastric cancer or gastroesophageal junction cancer (mGC/GEJC). Patients who have undergone gastrectomy constitute a significant proportion of patients with mGC/GEJC.

Objective: To assess the efficacy and safety of FTD/TPI among patients with previously treated mGC/GEJC who had or had not undergone gastrectomy.

Design, setting, and participants: This preplanned subgroup analysis of TAGS (TAS-102 Gastric Study), a phase 3, randomized, placebo-controlled, clinical trial included patients with mGC/GEJC who had received at least 2 previous chemotherapy regimens, and was conducted at 110 academic hospitals in 17 countries in Europe, Asia, and North America, with enrollment between February 24, 2016, and January 5, 2018; the data cutoff was March 31, 2018.

Interventions: Patients were randomized 2:1 to receive oral FTD/TPI 35 mg/m² twice daily or placebo twice daily with best supportive care on days 1 through 5 and days 8 through 12 of each 28-day treatment cycle.

Main outcomes and measures: The primary end point was overall survival. This subgroup analysis was conducted to examine potential trends and was not powered for statistical significance. Efficacy and safety end points were evaluated in the subgroups.

Results: Of 507 randomized patients (369 [72.8%] male; mean [SD] age, 62.5 [10.5] years), 221 (43.6%) had undergone gastrectomy (147 randomized to FTD/TPI and 74 to placebo) and 286 (56.4%) had not undergone gastrectomy (190 randomized to FTD/TPI and 96 to placebo). In the gastrectomy subgroup, the overall survival hazard ratio (HR) in the FTD/TPI group vs placebo group was 0.57 (95% CI, 0.41-0.79), and the progression-free survival HR was 0.48 (95% CI,

0.35-0.65). In the no gastrectomy subgroup, the overall survival HR in the FTD/TPI group vs placebo group was 0.80 (95% CI, 0.60-1.06), and the progression-free survival HR was 0.65 (95% CI, 0.49-0.85). Among FTD/TPI-treated patients, grade 3 or higher adverse events of any cause occurred in 122 of 145 patients (84.1%) in the gastrectomy subgroup and 145 of 190 (76.3%) in the no gastrectomy subgroup: 64 (44.1%) in the gastrectomy subgroup and 50 (26.3%) in the no gastrectomy subgroup had grade 3 or higher neutropenia, 31 (21.4%) in the gastrectomy subgroup and 33 (17.4%) in the no gastrectomy subgroup had grade 3 or higher anemia, and 21 (14.5%) in the gastrectomy subgroup and 10 (5.3%) in the no gastrectomy subgroup had grade 3 or higher leukopenia. In the gastrectomy subgroup, 94 (64.8%) had dosing modifications because of adverse events vs 101 (53.2%) in the no gastrectomy subgroup; 15 (10.3%) in the gastrectomy group and 28 (14.7%) in the no gastrectomy group discontinued treatment because of adverse events. Treatment exposure was similar between groups.

Conclusions and relevance: The FTD/TPI treatment was tolerable and provided efficacy benefits among patients with pretreated mGC/GEJC regardless of previous gastrectomy.



Josep Taberner, Maria Alsina, Kohei Shitara, Toshihiko Doi, Mikhail Dvorkin, Wasat Mansoor, Hendrik Tobias Arkenau, Aliaksandr Prokharau et al. Health-related quality of life associated with trifluridine/tipiracilin heavily pretreated metastatic gastric cancer: results from TAGS. *Gastric Cancer*. 2020; 23(4): 689–698

Abstract

Background: In TAGS, an international, double-blind, phase 3 trial, trifluridine/tipiracil significantly improved overall survival and progression-free survival compared with placebo in heavily pretreated metastatic gastric cancer patients. This paper reports pre-specified quality of life (QoL) outcomes for TAGS. **Methods:** Patients were randomized 2:1 to trifluridine/tipiracil (35 mg/m² twice daily on days 1-5 and 8-12 of each 28-day cycle) plus best supportive care (BSC) or placebo plus BSC. QoL was evaluated at baseline and at each treatment cycle, using the EORTC QLQ-C30 and EORTC QLQ-STO22 questionnaires; results were considered valid for analysis only if $\geq 10\%$ of patients completed the questionnaires. Key QoL outcomes were mean changes from baseline and time to

deterioration in QoL. A post hoc analysis assessed the association between QoL and time to deterioration of Eastern Cooperative Oncology Group performance score (ECOG PS) to ≥ 2 .

Results: Of 507 randomized patients, 496 had baseline QoL data available. The analysis cut-off was 6 cycles for trifluridine/tipiracil and 3 cycles for placebo. In both treatment groups, there were no clinically significant deteriorations in the mean QLQ-C30 Global Health Status (GHS) score, or in most subscale scores. In a sensitivity analysis including disease death and disease progression as events, there was a trend towards trifluridine/tipiracil reducing the risk of deterioration of QoL scores compared with placebo. Deterioration in the GHS score was associated with deterioration in ECOG PS.

Conclusion: QoL was maintained in TAGS, and there was a trend towards trifluridine/tipiracil reducing the risk of QoL deterioration compared with placebo.

ASCO ESMO

Abstract 3

Efficacy and safety of trifluridine/tipiracil in patients with metastatic gastric cancer with prior gastrectomy: Results from a phase 3 study (TAGS)

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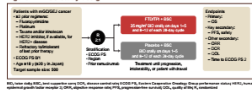
INTRODUCTION

- Standard of care for early-stage gastric cancer (GC) is surgery, the only potentially curative treatment¹
- 5-year survival rates after gastrectomy are ~40-50% in non-rare countries and ~30% or more in rare and lower²
- Disease recurs in at least 40-50% of patients³
- ~40% of patients with metastatic disease have had a previous gastrectomy^{4,5}
- Trifluridine (FTD)/tipiracil (TIP) is a novel oral therapy combining the thymidine analog trifluridine, and tipiracil, which prevents trifluridine degradation
- FTD/TIP is approved for treatment of metastatic colorectal cancer (mCRC)
- A phase 2, dose-toxicity study, EPOC020, evaluated FTD/TIP in patients with metastatic gastric cancer (mGC), with and without prior gastrectomy, after failure of standard chemotherapy⁶
- Median overall survival (OS) was 8.7 months (95% confidence interval [CI]: 5.7-11.9)
- We analyzed the efficacy and safety of FTD/TIP in patients with mGC/gastroesophageal junction (GEJ) cancer in the phase 3 study TAGS^{7,8}
- The impact of prior gastrectomy was evaluated in a pre-specified subgroup analysis

METHODS

- This randomized, double-blind, placebo-controlled, phase 3 study (NCT02000043; Figure 1) was conducted at 110 academic hospitals in 17 countries to evaluate the efficacy and safety of FTD/TIP versus placebo in previously treated patients with mGC of GEJ cancer
- Treatment continued until disease progression, intolerance, or patient withdrawal, the last date was March 31, 2018
- 354 events were targeted to observed detection of a hazard ratio (HR) for death of 0.70 with 90% power at a one-sided type 1 error of 0.025
- A planned analysis of subgroup was performed that included patients with gastrostomy, although these analyses were not powered for statistical significance

Figure 1. TAGS study design



RESULTS

- Patient population**
- Between February 24, 2016, and January 5, 2018, 507 patients were enrolled and randomized (trifluridine/tipiracil [TIP] group; 503 patients were treated [99.2%]; placebo group)
- Prior gastrectomy had been performed in:
 - 147 patients (44%) in the FTD/TIP group
 - 74 patients (44%) in the placebo group

Figure 2. OS and PFS in the overall study population

- Patient disposition and baseline demographic and disease characteristics (Table 1) were generally similar between patients with gastrostomy and the overall population
- Study treatment was discontinued in 94% and 100% of FTD/TIP-treated and placebo-treated patients, respectively, with prior gastrectomy, and in 94% and 94% of FTD/TIP-treated and placebo-treated patients in the overall population
- The most common reason for treatment discontinuation was disease progression (11% and 86% of FTD/TIP-treated and placebo-treated patients with prior gastrectomy; 73% and 86% of FTD/TIP-treated and placebo-treated patients in the overall population)
- Most patients with gastrostomy and in the overall population received ≥3 prior regimens

Table 1. Baseline demographic and disease characteristics

Characteristic	FTD/TIP (n=503)	Placebo (n=504)
Age, years	Median (range)	Median (range)
Sex, %		
Geographic region, %		
ECOG PS, %		
Number of metastatic sites, %		
Number of prior regimens, %		

Efficacy

- In the overall population, the primary study endpoint was met: FTD/TIP demonstrated a significant improvement in OS versus placebo (Figure 2)
- FTD/TIP also demonstrated a significant improvement in PFS versus placebo (Figure 2)
- Subgroup OS analyses favored the FTD/TIP group over the placebo group in most prespecified subgroups, including patients with previous gastrectomy (Figure 3)
- FTD/TIP-treated patients with gastrostomy tended to show OS and PFS benefits compared with placebo-treated patients with gastrostomy (Figure 4)
- Prior gastrectomy was not identified as a prognostic or predictive factor in multivariate Cox regression analyses, which included all prespecified factors
- Prognostic factors identified were ECOG PS as baseline stratification factor, age (<65 years vs ≥65 years), number of prior regimens, number of metastatic sites, and HER2 status at baseline
- None were found to be predictive
- Treatment effect was maintained the same after adjusting for all potential prognostic factors

Safety and tolerability

- In the FTD/TIP group, grade ≥3 AEs occurred in 84% of patients with gastrostomy and in 50% of the overall population (Table 2)
- FTD/TIP-treated patients with gastrostomy and in 58% of FTD/TIP-treated patients in the overall population, while treatment discontinuations due to AEs of any cause occurred in 10% and 13%, respectively (Table 2)
- Hematologic AEs appeared to be more frequent among FTD/TIP-treated patients with gastrostomy than among those in the overall population (Table 3)

Figure 3. OS subgroup analysis

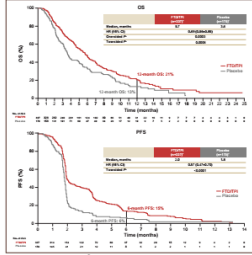


Table 2. Overall safety summary in patients with gastrostomy

Grade	FTD/TIP (n=503)	Placebo (n=504)
Any AE of any cause	99 (20%)	95 (19%)
Any treatment-related AE	88 (18%)	81 (16%)
Discontinuation due to AEs of any cause	50 (10%)	65 (13%)
Discontinuation due to treatment-related AEs	48 (10%)	61 (12%)

Figure 4. OS and PFS in patients with gastrostomy

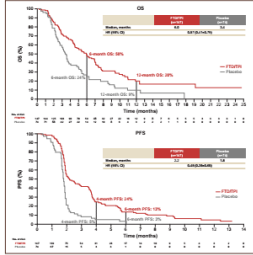


Table 3. Most common AEs in patients with gastrostomy

AE	FTD/TIP (n=503)	Placebo (n=504)
Hematologic AEs	80 (16%)	53 (11%)
Neutropenia without neutrophil count	53 (11%)	44 (9%)
Anemia without hemoglobin level	38 (8%)	23 (5%)
Leukopenia without leukocyte count	21 (4%)	16 (3%)
Thrombocytopenia without thrombocyte count	17 (3%)	13 (3%)
Other AEs	38 (8%)	36 (7%)
Diarrhea	30 (6%)	23 (5%)
Nausea	25 (5%)	23 (5%)
Vomiting	15 (3%)	13 (3%)
Abdominal pain	16 (3%)	12 (2%)
Constipation	12 (2%)	11 (2%)
Other AEs	35 (7%)	32 (6%)
Fatigue	25 (5%)	22 (4%)
Headache	21 (4%)	19 (4%)
Back pain	10 (2%)	11 (2%)

CONCLUSIONS

- FTD/TIP prolonged survival versus placebo regardless of gastrostomy
- Hematologic AEs such as neutropenia/thrombocytopenia may have been reported more frequent among FTD/TIP-treated patients with gastrostomy than in the overall population
- This did not result in more treatment discontinuations
- Exposure to FTD/TIP was similar between patients with gastrostomy and those in the overall population
- FTD/TIP is an effective treatment option with a manageable safety profile for patients with mGC, regardless of prior gastrectomy

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ANALYSIS OF SYMPTOMS AND FUNCTIONAL HRQoL SCALES IN TAGS, A PHASE III TRIAL OF TRIFLURIDINE/TIPIRACIL (FTD/TPI) IN METASTATIC GASTRIC CANCER (mGC)

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KEY TAKE-AWAYS

- This is the largest study in which health-related quality of life (HRQoL) was measured in patients with metastatic gastric cancer (mGC) receiving their third or subsequent line of treatment.
- HRQoL remained stable during the study for most functional and symptom scales in both arms, suggesting that HRQoL is largely maintained on treatment with trifluridine/tipiracil (FTD/TPI).
- There was a positive trend toward a lower risk of HRQoL deterioration with FTD/TPI versus placebo across most of the scores.
- Changes in HRQoL were significantly associated with patients' ECOG performance status, with patients with maintained HRQoL being more likely to have a maintenance of ECOG performance status.

BACKGROUND

- The oral chemotherapy FTD/TPI is recommended as third-line systemic therapy in patients with mGC. It was approved by the US Food and Drug Administration in February 2019 for adult patients with either mGC or gastroesophageal junction adenocarcinoma, previously treated with at least two lines of chemotherapy.²⁰
- FTD/TPI produced a clinically meaningful and statistically significant improvement in overall survival (OS) versus placebo in a randomized, double-blind, phase 3 trial (TAGS) in patients with heavily pretreated mGC.²¹
- It is important to assess the effect of cancer treatment on HRQoL, particularly in patients with limited life expectancy, for whom any survival benefits must be balanced against treatment toxicity and effects on HRQoL.²²
- The TAGS trial included assessment of the effect of FTD/TPI on HRQoL as a secondary endpoint; we report the results of these analyses here.

METHODS

- TAGS enrolled adult patients with mGC including adenocarcinoma of the gastroesophageal junction who had received at least two prior standard regimens for advanced disease, had an ECOG PS of 0 or 1 and who had progressed or were unable to tolerate their last previous therapy.²¹
- In combination with best supportive care, patients received either oral FTD/TPI 25 mg/m² twice daily on days 1-5 and 8-12 of a 28-day cycle or placebo.²¹
- HRQoL was evaluated using two European Organization for Research and Treatment of Cancer QoL questionnaires, the EORTC QLQ-C30 and the gastric cancer-specific EORTC QLQ-STO22, at baseline, prior to treatment administration on day 1 of each cycle from cycle 1 onwards and at the 28-day safety follow-up visit.²³
- QLQ scores and change in scores from baseline were determined for the summary scales, domain scales and single items. Changes in scores of ≥ 10 points were considered clinically relevant.²⁴ Results at time points for which $\geq 5\%$ of the total cohort completed questionnaires were considered valid for analysis.
- Time to deterioration of HRQoL was evaluated from the date of randomization. The treatment groups were compared using the stratified log-rank test and HR estimated using a stratified Cox proportional hazard model.²⁵
- In a pre-specified exploratory analysis, the association between deterioration in ECOG PS to a score of ≥ 2 and deterioration in HRQoL was investigated using a time-dependent Cox-regression analysis.²⁶

RESULTS

- A total of 507 patients were randomized to FTD/TPI (n=337) or placebo (n=170), with a median age of 64 and 80 years, respectively. Baseline demographic and disease characteristics were broadly similar between groups (reported in detail previously).²¹
- Baseline HRQoL data were available for 332 (98.5%) of FTD/TPI and 184 (96.5%) of placebo recipients. Baseline mean scores on both questionnaires were broadly similar between groups.

Questionnaire compliance

- Overall, the rate of questionnaire compliance was 84.0% for QLQ-C30 and 83.8% for QLQ-STO22 (Table 1).

Table 1. Quality of life questionnaire compliance rates for treatment cycles 1-6.

Type	EORTC QLQ-C30		EORTC QLQ-STO22	
	FTD/TPI (n=337)	Placebo (n=170)	FTD/TPI (n=337)	Placebo (n=170)
Overall	81.9	72.2	81.9	72.2
Cycle 1	84.9	78.7	84.6	78.7
Cycle 2	82.9	78.8	82.8	78.6
Cycle 3	77.3	74.8	76.7	74.8
Cycle 4	74.4	71.1	74.4	71.1
Cycle 5	72.9	67.1	73.9	67.1
Cycle 6	70.9	63.6	70.9	63.6

QLQ-C30: European Organization for Research and Treatment of Cancer QLQ-C30; QLQ-STO22: Quality of Life Questionnaire for Gastric Cancer QLQ-STO22. Quality of life.

Quality of life using QLQ-C30 scale

- In both the FTD/TPI and placebo groups, there were no clinically relevant changes in baseline HRQoL-C30 scores across most of the scales (Figure 2) or symptom scale (Figure 3).
- Differences between FTD/TPI and placebo in the mean change from baseline HRQoL-C30 scores were not clinically relevant, except for pain at cycle 2 (difference of 11.3 favoring FTD/TPI) and role functioning at cycle 3 (difference of 10.0 favoring placebo).

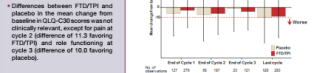
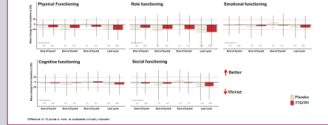


Figure 2. Change from baseline across treatment cycles in the EORTC QLQ-C30 functional scale scores.*



* High negative scores represent a lower HRQoL. 95% CI, 95% confidence interval.

Figure 3. Change from baseline across treatment cycles in the EORTC QLQ-C30 symptom scores.*



* High negative scores represent a lower HRQoL. 95% CI, 95% confidence interval.

Quality of life using QLQ-STO22 scale

- Changes from baseline in QLQ-STO22 scores were generally not clinically relevant in either treatment group, and there were no clinically relevant differences between groups over time for most items (Figure 4).

Figure 4. Change from baseline across treatment cycles in the QLQ-STO22 symptom scores.*



* High negative scores represent a lower HRQoL. 95% CI, 95% confidence interval.

ACKNOWLEDGEMENTS

We thank the patients and families who made this trial possible and provided data, nurses who were involved in the trial, as well as the data and safety monitoring board members. The TAGS trial was funded by Novartis. We thank Pharmacia for the Novartis Research Fellowship. We thank the sponsor and funding sponsor for their financial support in the preparation of this poster presented at the European Cancer Conference and the American Society of Clinical Oncology.

DISCLOSURES

Dr. Alonso: Novartis (Novartis). Dr. Taberner: Novartis (Novartis). Dr. Shihata: Novartis (Novartis). Dr. Doi: Novartis (Novartis). Dr. Dvornik: Novartis (Novartis). Dr. Massara: Novartis (Novartis). Dr. Arhin: Novartis (Novartis). Dr. Prokharau: Novartis (Novartis). Dr. Giallini: Novartis (Novartis). Dr. Favelin: Novartis (Novartis). Dr. Gortanova: Novartis (Novartis). Dr. Zhurav: Novartis (Novartis). Dr. Nishikawa: Novartis (Novartis). Dr. Ando: Novartis (Novartis). Dr. Yelton: Novartis (Novartis). Dr. Van Cutsem: Novartis (Novartis). Dr. Jiang: Novartis (Novartis). Dr. Legen: Novartis (Novartis). Dr. Salazar: Novartis (Novartis). Dr. Ross: Novartis (Novartis).

Time to deterioration in quality of life

- In a sensitivity analysis that included death or progressive disease (PD) as an event, FTD/TPI prolonged time to deterioration in GHS, versus placebo, versus deterioration was a reduction of 10 months on the QLQ-C30 GHS score (placeat ratio, HR=0.65; 95% CI, 0.52 to 0.81; Figure 5).
- The median time to deterioration by ≥ 10 points in QLQ-C30 GHS score was 2.11 months (95% CI, 2.07 to 2.17) for FTD/TPI versus 1.88 months (1.84 to 1.94) months for placebo.

Association between quality of life and time to ECOG performance status (PS) deterioration

- A reduction in the QLQ-C30 GHS score of ≥ 10 points was significantly associated with a deterioration in ECOG PS to a value of ≥ 2 (HR 1.21; 95% CI, 1.23 to 1.40), and similarly for all five QLQ-C30 functional scales (physical functioning, role functioning etc) and numerous individual items (Figure 6).
- At treatment discontinuation, 68% and 57% of the patients with ECOG PS=0-1 at baseline were recorded as being in PS=0 for HRQoL deterioration and placebo, respectively.

Figure 5. Time to deterioration in EORTC GHS score by 10 points was significantly associated with a deterioration in ECOG PS to a value of ≥ 2 .

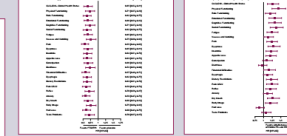


Figure 6. Forest plot showing the association between the time to deterioration in ECOG PS with time to deterioration in EORTC GHS score by 10 points in the ITT population (n=507).

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Презентации

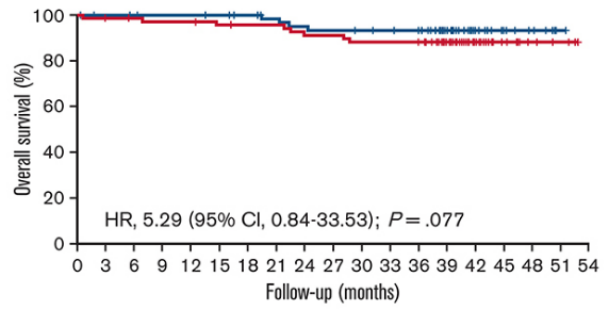
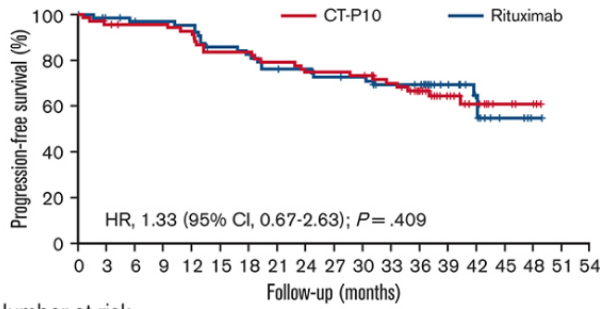
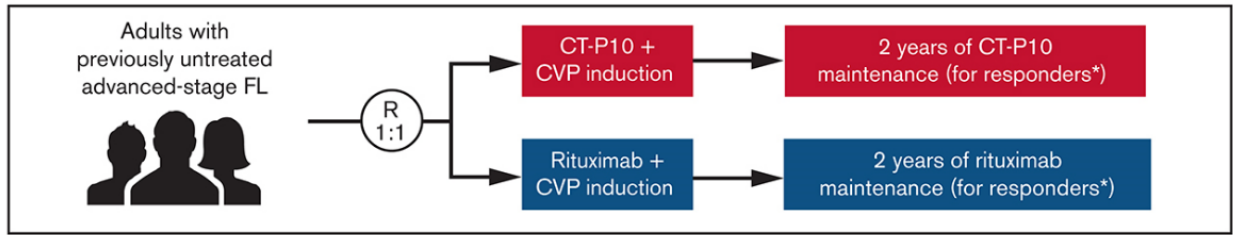
- ESMO-GI TAGS poster draft 13 Jun 2018
- LBA-002 ESMO-GI TAGS poster
- ESMO-GI 2018 TAGS oral draft 20Jun2018 FINAL
- Dr Thuss TAGS Gastrektomie Vortragenswurf 10 09 2019 Thu JHe

A Phase 3, Randomized, Parallel-Group, Active-Controlled, Double-Blind Study to Compare Efficacy and Safety between CTP10 and Rituxan in Patients with Low Tumour Burden Follicular Lymphoma

Christian Buske, Wojciech Jurczak, Juan-Manuel Sancho, Edvard Zhavrid, Jin Seok Kim, José-Ángel Hernández-Rivas, Aliaksandr Prokharau et al. Long-term efficacy and safety of CT-P10 or rituximab in untreated advanced follicular lymphoma: a randomized phase 3 study. *Blood Adv* (2021) 5 (17): 3354–3361.



Long-term efficacy and safety of CT-P10 or rituximab in untreated advanced FL: randomized phase 3 study



Number at risk

CT-P10	70	66	64	64	62	56	56	53	50	50	49	43	35	23	14	5	3	0
Rituximab	70	64	62	61	60	53	51	47	46	43	42	38	37	20	13	4	1	0

	70	68	67	66	66	64	63	63	60	60	58	58	57	45	28	12	5	3	0
	70	68	67	66	66	64	62	59	57	56	55	54	52	38	22	13	8	2	0

After a median follow-up of 39.9 months, time-to-event analyses demonstrated comparability between CT-P10 and rituximab

Overall long-term safety profiles were comparable between CT-P10 and rituximab

CI, confidence interval; CVP, cyclophosphamide, vincristine, and prednisone; FL, follicular lymphoma; HR, hazard ratio; R, randomization.
 *Patients achieving complete response, unconfirmed complete response, or partial response after week 24 of the induction period.



Bertrand Coiffier, Juan-Manuel Sancho, Wojciech Jurczak, Jin Seok Kim, Raj V Nagarkar, Edvard Zhavrid, Jose Angel Hernandez Rivas, Aliaksandr Prokharau, Pharmacokinetic and Safety of CT-P10, a Biosimilar Candidate to the Rituximab Reference Product, in Patients with Newly Diagnosed Advanced Stage Follicular Lymphoma (AFL) *Blood* (2016) 128 (22): 1807.

Abstract

Background: CT-P10 is a biosimilar candidate to the reference rituximab product, EU-approved MabThera® and US-licensed Rituxan®. CT-P10 has an identical amino acid sequence and highly similar physicochemical and in vitro functional properties to its reference drug. In patients with rheumatoid arthritis, CT-P10 has demonstrated compelling similarity in pharmacokinetics (PK), pharmacodynamics (PD), efficacy, safety and immunogenicity (Yoo DH, et al. *Arthritis Rheum.* 2013;65(10):1736).

Objective: The goal of this study was to demonstrate PK similarity of CT-P10 to rituximab, each administered in combination with cyclophosphamide, vincristine, and prednisone (CVP) in patients with newly diagnosed Advanced Follicular Lymphoma (AFL) (NCT02162771) (Kim WS et al. *Blood.* 2015;126(23): 5111). The results of PK, PD, safety and immunogenicity up to Core Cycle 4 (12 weeks) are presented here from this ongoing study.

Methods: Patients with AFL were randomized 1:1 to receive infusion (375mg/m²) of either CT-P10 or rituximab, at a 3-week interval, in combination with CVP. PK analysis was conducted in terms of AUC_{tau} and C_{max} at steady state, Core Cycle 4, as primary PK endpoints. PK parameter values considered as outliers determined by robust regression outlier testing were excluded from the pharmacokinetic primary analysis.

Results: In total, 121 patients were randomly assigned to receive either CT-P10 (n=59) or rituximab (n=62) in combination with CVP. Result of CT-P10 PK at Core Cycle 4 was similar to that of rituximab. The ratios (90% CI) of geometric least square means (CT-P10 to rituximab treatment group) were 102.3% (94.1%-111.2%) for AUC_{tau} and 100.7% (93.8%-108.0%) for C_{max}SS at Core Cycle 4. The 90% CIs of ratio of geometric LS means for both AUC_{tau} and C_{max}SS were entirely contained within the equivalence margin of 80% to 125% (Table 1 and Figure 1). Mean serum concentrations of the study drug were highly similar for the 2 treatment groups at each time point (Core Cycle 1 to 4).

The B-cell kinetics was similar up to Core Cycle 4 in the 2 treatment groups. Median number of B-cells decreased to below the lower limit of quantification

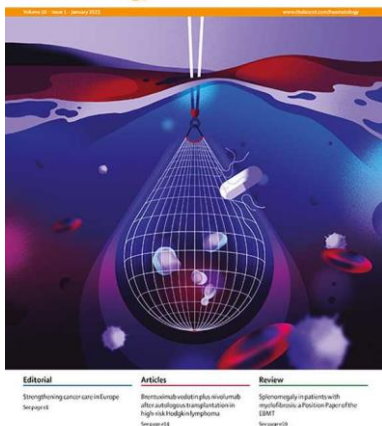
(LLoQ) (20 cells/ μ L) 1 hour after the end of infusion at Core Cycle 1 and remained below the LLoQ at each subsequent cycle, up to and including Core Cycle 4.

The proportion of patients with a positive anti-drug antibody up to Core Cycle 4 at post-treatment visits was similar between the 2 treatment groups; 3/59 (5.1%) patients and 2/62 (3.2%) patients in the CT-P10 and rituximab groups, respectively.

In addition, CT-P10 was well tolerated and the safety profile of CT-P10 up to Core Cycle 4 was similar to that of rituximab. The number of patients who experienced at least 1 treatment emergent adverse event (TEAE) was 43 (72.9%) patients and 41 (66.1%) patients in CT-P10 and rituximab treatment groups, respectively. The proportion of patients who experienced at least 1 treatment emergent serious adverse event considered by the investigator to be related to the study treatment was similar between the 2 treatment groups; 2/59 (3.4%) patients and 2/62 (3.2%) patients in the CT-P10 and rituximab groups, respectively. The frequencies of adverse events special interest (AESI) were similar between the 2 treatment groups (Table 2).

Conclusion: This study demonstrated similarity of PK in terms of AUC_{tau} and C_{max}SS between CT-P10 and rituximab in AFL patients. The B-cell kinetics and immunogenicity were comparable between the two treatment groups. CT-P10 was well tolerated with a safety profile comparable to that of rituximab up to and including Core Cycle 4 (12 weeks).

THE LANCET
Haematology



Won Seog Kim, Christian Buske, Michinori Ogura, Wojciech Jurczak, Juan-Manuel Sancho, Edvard Zhavrid, Jin Seok Kim, José-Ángel Hernández-Rivas, Aliaksandr Prokharau et al. Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 compared with rituximab in patients with previously untreated advanced-stage follicular lymphoma: a randomised, double-blind, parallel-group, non-inferiority phase 3 trial. *Lancet Haematol.* 2017 Aug;4(8):e362-e373

Abstract

Background: Studies in patients with rheumatoid arthritis have shown that the rituximab biosimilar CT-P10 (Celltrion, Incheon, South Korea) has equivalent efficacy and pharmacokinetics to rituximab. In this phase 3 study, we aimed to assess the non-inferior efficacy and pharmacokinetic equivalence of CT-P10 compared with rituximab, when used in combination with cyclophosphamide, vincristine, and prednisone (CVP) in patients with newly diagnosed advanced-stage follicular lymphoma.

Methods: In this ongoing, randomised, double-blind, parallel-group, active-controlled study, patients aged 18 years or older with Ann Arbor stage III-IV follicular lymphoma were assigned 1:1 to CVP plus intravenous infusions of 375 mg/m² CT-P10 or rituximab on day 1 of eight 21-day cycles. Randomisation was done by the investigators using an interactive web or voice response system and a computer-generated randomisation schedule, prepared by a clinical research organisation. Randomisation was balanced using permuted blocks and was stratified by country, gender, and Follicular Lymphoma International Prognostic Index score (0-2 vs 3-5). Study teams from the sponsor and clinical research organisation, investigators, and patients were masked to treatment assignment. The study was divided into two parts: part 1 assessing equivalence of pharmacokinetics (in the pharmacokinetics subset), and part 2 assessing efficacy in all randomised patients (patients from the pharmacokinetics subset plus additional patients enrolled in part 2). Equivalence of pharmacokinetics was shown if the 90% CIs for the geometric mean ratio of CT-P10 to rituximab in AUC_τ and C_{maxSS} were within the bounds of the equivalence margin of 80% and 125%. Non-inferiority of response was shown if the one-sided 97.5% CI lay on the positive side of the -7% margin, using a one-sided test done at the 2.5% significance level. The primary efficacy endpoint was the proportion of patients who had an overall response over eight cycles and was assessed in the efficacy population (all randomised patients). The primary pharmacokinetic endpoints were area under the serum concentration-time curve at steady state (AUC_τ) and maximum serum concentration at steady state (C_{maxSS}) at cycle 4, assessed in the pharmacokinetic population.

Findings: Between July 28, 2014, and Dec 29, 2015, 140 patients were enrolled. Here we report data for the eight-cycle induction period, up to week 24. The proportion of patients with an overall response in the efficacy population was 64 (97.0%) of 66 patients in the CT-P10 treatment group and 63 (92.6%) of 68 patients in the rituximab treatment group (4.3%; one-sided 97.5% CI -4.25), which lay on the positive side of the predefined non-inferiority margin. The ratio of geometric least squares means (CT-P10/rituximab) was 102.25% (90% CI 94.05-111.17) for AUC_τ and 100.67% (93.84-108.00) for C_{maxSS}, with all CIs within the

bioequivalence margin of 80-125%. Treatment-emergent adverse events were reported for 58 (83%) of 70 patients in the CT-P10 treatment group and 56 (80%) of 70 in the rituximab treatment group. The most common grade 3 or 4 treatment-emergent adverse event in each treatment group was neutropenia (grade 3, 15 [21%] of 70 patients in the CT-P10 group and seven [10%] of 70 patients in the rituximab group). The proportion of patients who experienced at least one treatment-emergent serious adverse event was 16 (23%) of 70 patients in the CT-P10 group and nine (13%) of 70 patients in the rituximab group.

Interpretation: In this study, we show that CT-P10 exhibits non-inferior efficacy and pharmacokinetic equivalence to rituximab. The safety profile of CT-P10 was comparable to that of rituximab. CT-P10 might represent a new therapeutic option for advanced-stage follicular lymphoma.

A Randomized, Double Blind, Multicenter, Parallel-Group, Phase III Study to Evaluate Efficacy and Safety of DCVAC/PCa Versus Placebo in Men with Metastatic Castration Resistant Prostate Cancer Eligible for 1st Line Chemotherapy

JAMA Oncology

Nicholas J. Vogelzang, MD; Tomasz M. Beer, MD; Winald Gerritsen, MD; Stéphane Oudard, MD; Pawel Wiechno, MD, PhD; Bozena Kukielka-Budny, MD, PhD; Vladimir Samal, MD, PhD; Jaroslav Hajek, MD; Susan Feyerabend, MD; Vincent Khoo, MD; Arnulf Stenzl, MD; Tibor Csöszi, MD; Zoran Filipovic, MD; Frederico Goncalves, MD; Alexander Prokhorov, MD et al. *JAMA Oncol.* 2022; 8(4):546-552

Key Points

Question What is the efficacy and safety of DCVAC/PCa, an active cellular immunotherapy, in men with metastatic castration-resistant prostate cancer (mCRPC)?

Findings In this randomized clinical trial of 1182 patients, there was no difference in overall survival (OS) between the DCVAC/PCa and placebo groups, with median OS of 23.9 and 24.3 months, respectively. Treatment-emergent adverse events related to DCVAC/PCa or placebo occurred in 9.2% and 12.7% of patients, respectively.

Meaning DCVAC/PCa combined with docetaxel plus prednisone and continued as maintenance treatment did not extend OS and was well tolerated in patients with mCRPC; factors associated with the efficacy of immunotherapy should be identified to better select patients and thus prolong OS.

Abstract

Importance DCVAC/PCa is an active cellular immunotherapy designed to initiate an immune response against prostate cancer.

Objective To evaluate the efficacy and safety of DCVAC/PCa plus chemotherapy followed by DCVAC/PCa maintenance treatment in patients with metastatic castration-resistant prostate cancer (mCRPC).

Design, Setting, and Participants The VIABLE double-blind, parallel-group, placebo-controlled, phase 3 randomized clinical trial enrolled patients with mCRPC among 177 hospital clinics in the US and Europe between June 2014 and November 2017. Data analyses were performed from December 2019 to July 2020.

Interventions Eligible patients were randomized (2:1) to receive DCVAC/PCa (add-on and maintenance) or placebo, both in combination with chemotherapy (docetaxel plus prednisone). The stratification was applied according to geographical region (US or non-US), prior therapy (abiraterone, enzalutamide, or neither), and Eastern Cooperative Oncology Group performance status (0-1 or 2). DCVAC/PCa or placebo was administered subcutaneously every 3 to 4 weeks (up to 15 doses).

Main Outcomes and Measures The primary outcome was overall survival (OS), defined as the time from randomization until death due to any cause, in all randomized patients. Survival was compared using 2-sided log-rank test stratified by geographical region, prior therapy with abiraterone and/or enzalutamide, and Eastern Cooperative Oncology Group performance status.

Results A total of 1182 men with mCRPC (median [range] age, 68 [46-89] years) were randomized to receive DCVAC/PCa (n = 787) or placebo (n = 395). Of these, 610 (81.8%) started DCVAC/PCa, and 376 (98.4%) started placebo. There was no difference in OS between the DCVAC/PCa and placebo groups in all randomized patients (median OS, 23.9 months [95% CI, 21.6-25.3] vs 24.3 months [95% CI, 22.6-26.0]; hazard ratio, 1.04; 95% CI, 0.90-1.21; *P* = .60). No differences in the secondary efficacy end points (radiological progression-free survival, time to prostate-specific antigen progression, or skeletal-related events) were observed. Treatment-emergent adverse events related to DCVAC/PCa or placebo occurred in 69 of 749 (9.2%) and 48 of 379 (12.7%) patients, respectively. The most common treatment-emergent adverse events (DCVAC/PCa [n = 749] vs placebo [n = 379]) were fatigue (271 [36.2%] vs 152 [40.1%]), alopecia (222 [29.6%] vs 130 [34.3%]), and diarrhea (206 [27.5%] vs 117 [30.9%]).

Conclusions and Relevance In this phase 3 randomized clinical trial, DCVAC/PCa combined with docetaxel plus prednisone and continued as maintenance treatment did not extend OS in patients with mCRPC and was well tolerated.

«Разработка технологии выявления риска онкологических заболеваний на основе эпигенетических и молекулярно-генетических маркеров». Программа союзного государства 2017- 2021 г.

- Алгоритм прогнозирования НМРЛ на основе клинических и молекулярных предикторов. ГПНИ (государственная программа научных исследований) 2021-2023 гг.
- Алгоритм определения субклинического рецидива немелкоклеточного рака легкого на основе морфологических и молекулярно-генетических маркеров опухолевых клеток. ГПНИ (государственная программа научных исследований) 2020-2022 гг.

Совместно с институтом генетики НАН РБ изучены дополнительные критерии риска возникновения немелкоклеточного рака легкого на основе молекулярно-генетических особенностей пациентов. Работа проводится по двум темам: «Алгоритм определения субклинического рецидива на основе морфологических и молекулярно-генетических маркеров опухолевых клеток» (2020) и «Алгоритм прогнозирования НМР на основе клинических и молекулярных предикторов» (2021 г. - по наст. время).

**Неотложная
кардиология**

и кардиоваскулярные риски

ISSN 2616-633X

Шепетько М.Н., Мириленко Л.В., Прохоров А.В. Влияние выраженности бронхиальной обструкции на выживаемость пациентов с немелкоклеточным раком легкого после хирургического лечения. Неотложная кардиология и кардиоваскулярные риски. (2022); Том. 6. №1. С. 1519-1524.

Рак легкого представляет медико-социальную проблему. Показатели функции внешнего дыхания (ФВД), которые были получены в результате спирометрии, статистически значимо влияют на общую выживаемость пациентов с немелкоклеточным раком легкого.

Цель исследования: установить роль показателей, характеризующих степень бронхиальной обструкции у пациентов с немелкоклеточным раком легкого I-III стадий и оценить её влияние на выживаемость пациентов после хирургического лечения.

Материал исследования: в исследование включены 303 пациента с немелкоклеточным раком легкого (НМРЛ) I-III стадий, получивших лечение в УЗ «Минский городской клинический онкологический центр» с 2000 по 2018 гг., у которых были определены показатели ФВД и прослежены отдалённые результаты лечения.



Mikhail N.Shapetska, Evelina V.Krupnova, Alena P.Mikhaleuka, Natalia V.Chebotareva, Anna N.Shchayuk, Svetlana G.Pashkevich, Alexander V.Prokhorov. Prognostic Significance of Comparison of Clinical Indicators with Manifestations of Genetic Polymorphism of Glutathione-S-Transferases in Non-Small Cell Lung Cancer. Journal of Cancer Therapy, 2018, 9, 962-973.

Abstract

The article presented the results of comparison of polymorphic variants of the genes GSTM1, GSTT1, GSTP1 and clinical manifestations of non-small cell lung carcinoma. The association of the genotype GSTT1 (del) with the risk of developing squamous cell lung cancer has been revealed (OR = 2.54 CI: 1.13 - 5.72, $p = 0.035$). Analysis of patient survival rate ($n = 173$) in groups of various histological types of lung cancer showed that in the group of squamous cell lung cancer ($n = 91$) in patients with genotype GSTT1 (del), the survival rate median was significantly higher—84 months (95% CI 12.4 - 155.7) than in patients with the genotype GSTT1 (+)—36 months (95% CI 25.2 - 46.8, $p = 0.045$). In contrast, in the adenocarcinoma group ($n = 82$), the survival rate median in patients with the genotype GSTT1 (del) was 19 months. (95% CI 6.2 - 33.5), and in patients with genotype GSTT1 (+)—67 months (95% CI 50.1 - 84.0), which is the basis for continuing this comparison in an additional group of testees, as the sampling did not achieve the reliability of $p = 0.12$. Hypothetically, these differences may be due to differences in the gender composition of squamous cell lung cancer and adenocarcinoma and the involvement of GST enzymes in the metabolism of estrogens in adenocarcinoma in women and other hormonal background and reactivity of the male body with squamous cell carcinoma. Further research and subsequent analysis of the results will be aimed at confirming this hypothesis.

- Шепетько М.Н., Крупнова Э.В., Михаленко Е.П., Чеботарева Н.В., Щаюк А.Н., Прохоров А.В Влияние генетического полиморфизма глутатион-s-трансфераз при немелкоклеточном раке легкого. В сборнике: Хирургия Беларуси на современном этапе. материалы XVI съезда хирургов Республики Беларусь и Республиканской научно-практической конференции: в 2 частях. 2018. С. 65-67.

Основная (инициативная) тема НИР кафедры (2023-2026 гг.) «Современные методы обследования и комплексное лечение злокачественных гастроинтестинальных и урогенитальных опухолей»



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Research Article

Open Access

Gastroesophageal Cancer: Prognostic Factors and Treatment Results

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Abstract

The study presents the remote results of surgical treatment of 329 patients with cancer of gastroesophageal localization. Three 3-year survival rate is 37.1%, the 5-year survival rate is 26.2%. Prognosis after the surgery depends primarily on the extent of the tumour spread. In all types of surgeries the survival rate of patients without lymph nodes metastasis is twice as high as that of patients with metastatic spread to lymph nodes. The amount of the affected lymph nodes does not affect overall as well as relapse-free survival. Combined and palliative resections may procedure the 5-year survival rate at the level of only 10-15%.

Keywords: Gastroesophageal cancer; Surgical treatment; Survival rate; Remote treatment results



JSM Surgical Oncology and Research

Research Article

First Experience of Using the Technique of declipseSPECT for Preoperational Visualization of Sentinel Lymph Nodes with Malignant Tumors

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Keywords

- Sentinel lymph node
- Technique of declipseSPECT
- Breast cancer
- Skin melanoma
- Thyroid cancer
- Endometrial
- Vulvar cancer

Abstract

The article presents the results of the first experience of using the technique of declipseSPECT for detection of sentinel lymph nodes with different-localization malignant tumors. The technique of declipseSPECT was used in patients with breast cancer, melanoma skin, thyroid, endometrial and vulvar cancer. In the current study a lyophilized powder was used to prepare a technetium (99mTc) mill microspheres solution, whose active substance is human albumin of 100-600 nm.

The highest accuracy, specificity and sensitivity of the technique were seen in patients with breast cancer, skin melanoma, endometrial and vulvar cancer. A low informative value of the technique was observed in thyroid cancer. To our opinion, this is due to a large number of lymph nodes compartments in the neck region and due to sentinel lymph nodes of different localization. A further study of the efficiency of this technique of visualization of a sentinel lymph node, mainly in breast cancer, will permit one not to use preventive axillary lymph node dissection and to improve the quality of the patient's life.



Прохоров АВ, Лабунец ИН, Мавричев ВЮ, Тур ГЕ, Гедевич ЗЭ, Адамцевич МА. Результаты хирургических вмешательств при раке желудка и пищевода с формированием безаппаратных пищеводных анастомозов. Онкологический журнал, 2019 Vol.13, Issue 4, P. 12-17

Целью данной работы является изучение непосредственных и ближайших результатов используемой нами инвагинационной методики формирования безаппаратного ручного пищеводно-желудочного и пищеводно-кишечного анастомоза при хирургическом лечении рака желудка и пищевода.

Материал и методы. Ретроспективно проанализированы результаты 1246 операций с использованием методики формирования пищеводного соустья без использования сшивающих аппаратов, произведенных по поводу рака пищевода и желудка, выполненный в Минском городском онкологическом диспансере за период с 2003 по 2018 год. Выполнялись следующие виды операций: 714 пациентам произведена гастрэктомия по Савиных, 64 пациентам - проксимальная резекция желудка по Савиных. Гастрэктомия по Осава-Гэрлоку выполнена у 209 пациентов, субтотальная проксимальная резекция желудка с нижней третью пищевода по Осава-Гэрлоку - 135 пациентам. Субтотальная резекция пищевода с одномоментной гастроэзофагопластикой по Льюису произведена у 124 пациентов.

Результаты. Послеоперационные осложнения наблюдались в 6,7% случаев, госпитальная летальность составила 3,5%. Наиболее часто наблюдались осложнения терапевтического профиля, не связанные непосредственно с хирургической техникой. Несостоятельность швов пищеводного анастомоза (НША) наблюдалась в 9 случаях (10,7% всех осложнений). При этом непосредственной причиной смерти она явилась в 6 случаях (13,6% от общего числа умерших). После выписки из клиники в ближайшие и отдаленные сроки у 74 пациентов (5,9%) зафиксированы явления рубцового стеноза пищеводного анастомоза. Выраженных органических и функциональных нарушений со стороны пищеводных анастомозов в виде рубцово-язвенных деформаций и стриктур, требующих хирургической коррекций, не наблюдалось.

Выводы. Частота несостоятельности пищеводно-желудочного и пищеводно-тонкокишечного анастомоза, выполненного с использованием однотипной

инвагинационной методики путем наложения ручных отдельных узловых швов, составляет 0,7% от общего числа произведенных операций с летальностью от данного осложнения 0,5%. Возможность развития несостоятельности пищеводного соустья не сопряжена с характером произведенной операции, её объёмом и уровнем резекции пищевода и полностью зависит от хирургической техники исполнения.

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«Персонализированное лечение карциносаркомы эндометрия (экспериментально-клиническое исследование) 2016-2020 гг.

В исследовании впервые установлено, что медленный рост заболеваемости злокачественными опухолями тела матки в Беларуси связан скорее всего с влиянием аварии на ЧАЭС, из-за которой через 30 лет этот показатель увеличился в загрязненных районах в 3,6-4,3 раза. Одновременно произошло увеличение заболеваемости крайне редко встречающейся в стране карциносаркомой эндометрия (КСЭ) в 7,5 раза в РБ и в 13,9 в г. Минске. Впервые изучено гистологическое строение КСЭ, определена ее 5-летняя выживаемость и локализация метастазов. Предложена адъювантная лазерная гемотерапия для улучшения результатов комплексной терапии КСЭ, противоопухолевое действие которой подтверждено в эксперименте *in vivo*. Доказано, что оптимальным методом для стадирования КСЭ и рака шейки матки является ДВИ МРТ. Установлено, что экспрессия онкогенов p53 >60% и bcl-2 >11 после химиолучевой терапии свидетельствует о возможной неизлеченности опухолевого процесса при местно-распространенном раке шейки матки или о появлении в течении 3-х лет рецидивов или метастазов.

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