European Journal of Cancer 97 (2018) 16–24

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Geriatric analysis from PRODIGE 20 randomized phase II trial evaluating bevacizumab + chemotherapy versus chemotherapy alone in older patients with untreated metastatic colorectal cancer☆

T. Aparicio [a,*], O. Bouché [b], E. Francois [c], F. Retornaz [d], E. Barbier [e], J. Taieb [f], S. Kirscher [g], P.-L. Etienne [h], R. Faroux [i], F. Khemissa Akouz [j], F. El Hajbi [k], C. Locher [l], Y. Rinaldi [m], T. Lecomte [n], S. Lavau-Denes [o], M. Baconnier [p], A. Oden-Gangloff [q], D. Genet [r], L. Bedenne [s], E. Paillaud [t], for PRODIGE 20 investigators[1]

[a] *Gastroenterology Department, CHU Saint Louis, APHP and Université Paris 7, Sorbonne Paris Cité, Paris, France*
[b] *Digestive Oncology Department, CHU Robert Debré, Reims, France*
[c] *Gastroenterology Department, Centre Antoine Lacassagne, Nice, France*
[d] *Geriatric Department, Hôpital Européen, Marseille, France*
[e] *Statistics Department, Fédération Francophone de Cancérologie Digestive, Dijon, France*
[f] *Digestive Oncology Department, CHU Georges Pompidou, APHP, Paris, France*
[g] *Oncology Department, Institut Sainte Catherine, Avignon, France*
[h] *Oncology Department, CARIO, HPCA, Plérin, France*
[i] *Gastroenterology Department, CHG Vendée, La Roche sur Yon, France*
[j] *Gastroenterology Department, CH Saint Jean, Perpignan, France*
[k] *Oncology Department, Centre Oscar Lambret, Lille, France*
[l] *Gastroenterology Department, CH Meaux, Meaux, France*
[m] *Gastroenterology Department, Hôpital Européen, Marseille, France*
[n] *Gastroenterology Department, CHU Trousseau, Tours, France*
[o] *Oncology Department, CHU Dupuytren, Limoges, France*
[p] *Gastroenterology Department, CH Annecy Genevois, Pringy, France*
[q] *Gastroenterology Department, CHU Charles Nicolle, Rouen, France*
[r] *Oncology Department, Clinique Chenieux, Limoges, France*
[s] *Gastroenterology Department, CHU Le Bocage, INSERM U 866, Dijon, France*
[t] *Geriatric Department, CHU Henri Mondor, APHP, Créteil, France*

Received 24 August 2017; received in revised form 19 March 2018; accepted 27 March 2018

☆ **Previous presentation:** This work was presented at the annual ESMO meeting in 2016 and SIOG meeting in 2017.

* *Corresponding author*: Gastroenterology Department, Saint Louis Hospital, AP-HP, Université Paris 7, Sorbonne Paris Cité, 1 Avenue Claude Vellefaux, 75010 Paris, France. Fax: +33 1 42 49 91 68.
E-mail address: thomas.aparicio@aphp.fr (T. Aparicio).

[1] Please see the Supplementary Appendix for a list of the PRODIGE 20 Investigators/collaborators.

https://doi.org/10.1016/j.ejca.2018.03.030

KEYWORDS
Geriatric assessment;
Colon cancer;
Predictive factors;
Bevacizumab;
Elderly

Abstract ***Background:*** Older patients have frailty characteristics that impair the transposition of treatment results found in younger patients. Predictive factors are needed to help with treatment choices for older patients. The PRODIGE 20 study is a randomized phase II study that evaluated chemotherapy associated with bevacizumab (BEV) or not (CT) in patients aged 75 years or older.
Patients and methods: Patients underwent a geriatric assessment at randomization and at each evaluation. The predictive value of geriatric and oncologic factors was determined for the primary composite end-point assessing safety and efficacy of treatment (BEV or CT) simultaneously and also progression-free survival (PFS) and overall survival (OS).
Results: 102 patients were randomized (51 BEV and 51 CT; median age 80 years [range 75–91]). On multivariate analysis, baseline normal independent activity of daily living (IADL) score and no previous cardiovascular disease predicted the primary end-point. High (versus low) baseline Köhne score predicted short PFS and baseline Spitzer quality of life (QoL) score <8, albumin level ≤ 35 g/L, CA19.9 >2 LN levels above normal and high baseline Köhne score predicted short OS. Survival without deteriorated QoL and autonomy was similar with BEV and CT. On subgroup analyses, the benefit of bevacizumab seemed to be maintained in patients with baseline impaired IADL or nutritional status.
Conclusion: Normal IADL score was associated with a good efficacy and safety of both BEV and CT. Köhne criteria may be relevant prognostic factors in older patients. Adding bevacizumab to chemotherapy does not impair patient autonomy or QoL.

1. Introduction

About 40% of colorectal cancer (CRC) cases are diagnosed in patients older than 75 years [1]. Thus, the management of cancer in older adults represents an important part of everyday oncology practice. The treatment choice for older patients with CRC remains a challenge because of a number of unresolved issues [2]. Indeed, evidence-based medicine is established from trials that involved a small number or highly selected older patients, and the enrolment rate dropped markedly after the age of 75 years [3,4]. Older cancer patients constitute a heterogeneous population with various combinations of comorbidities, disabilities, and geriatric syndromes.

Geriatric assessment (GA) was developed to detect geriatric conditions and disabilities that can contribute to frailty in older patients. GA involves evaluating the patient's functional status, mobility, comorbidities, polypharmacy, nutritional status, cognitive function, emotional status, and social support with validated geriatric tools [5]. Specific prognostic factors of poor survival have been described in older patients with various cancers and include dependence on the Instrumental Activities of Daily Living (IADL) scale, poor quality of life (QoL), depressive symptoms and cognitive decline [6]. Nevertheless, the predictive ability of GA for treatment toxicity or mortality has been reported with variability [7]. Only one prospective trial evaluated GA in one homogenous older population with metastatic CRC (mCRC) [8,9]. In this trial, cognitive and functional impairments predicted severe toxicity or unexpected hospitalization, and functional impairment predicted overall survival (OS).

Two phase III trials comparing capecitabine alone or with bevacizumab focused on older patients. Both reported improved progression-free survival (PFS) with BEV [10,11], without significant improvement in overall survival (OS). Unfortunately, the studies did not perform specific GA. Moreover, the effect of bevacizumab on autonomy or QoL has not been explored in previous randomized trials of older patients.

The PRODIGE 20 trial was a randomized phase II study evaluating infusion chemotherapy with (BEV) or without bevacizumab (CT) in patients with mCRC aged 75 years or older. Treatment with the anti-angiogenic BEV was safe and efficient [12]. The purpose of this ancillary study was to (1) determine predictive and prognostic factors in this specific geriatric population by assessing both commonly used oncologic and geriatric parameters and (2) estimate survival without deteriorated autonomy and QoL.

2. Patients and methods

2.1. Patient selection

The eligibility criteria were histologically confirmed unresectable mCRC, age ≥ 75 years, Eastern Cooperative Oncology Group (ECOG) score ≤ 2, ≥ 1 measurable