Cetuximab Pharmacokinetics Influences Progression-Free Survival of Metastatic Colorectal Cancer Patients

Titre	Cetuximab Pharmacokinetics Influences Progression-Free Survival of Metastatic Colorectal Cancer Patients
Type de publication	Article de revue
Auteur	Azzopardi, Nicolas [1], Lecomte, Thierry [2], Ternant, David [3], Boisdron-Celle, Michèle [4], Piller, Friedrich [5], Morel, Alain [6], Gouilleux-Gruart, Valérie [7], Vignault-Desvignes, Céline [8], Watier, Hervé [9], Gamelin, Erick [10], Paintaud, Gilles [11]
Editeur	American Association for Cancer Research
Type	Article scientifique dans une revue à comité de lecture
Année	2011
Langue	Anglais
Date	2011/01/10
Numéro	19
Pagination	6329 - 6337
Volume	17
Titre de la revue	Clinical Cancer Research
ISSN	1078-0432
Résumé en anglais	Purpose: An ancillary phase II study was conducted to study interindividual variability in cetuximab pharmacokinetics and its influence on progression-free survival (PFS) in metastatic colorectal cancer patients cotreated with irinotecan and 5-fluorouracil. Experimental Design: Ninety-six patients received cetuximab as an infusion loading dose of 400 mg/m2 followed by weekly infusions of 250 mg/m2. Doses of irinotecan and 5-fluorouracil were adjusted individually. Cetuximab concentrations were measured by ELISA. Compartmental pharmacokinetic parameters were estimated by a population approach, and PFS was analyzed using a Cox model. Results: Cetuximab pharmacokinetics was best described using a two-compartment model with both first-order and saturable (zero-order) elimination. Estimated pharmacokinetic parameters (% standard error) were as follows: central volume of distribution V1 = 2.96 L (4%), peripheral volume of distribution V2 = 4.65 L (6%), elimination clearance CL = 0.497 L/d (4%), distribution clearance Q = 0.836 L/d (8%), and zero-order elimination rate k0 = 8.71 mg/d (10%). Body surface area influenced V1, V2, and k0. Pretreatment serum albumin influenced CL. Risk of disease progression decreased with cetuximab global clearance (cumulative dose/cumulative area under the concentration versus time curve; P = 0.00016). Median PFS of patients with a cetuximab residual concentration on day 14 below median value was 3.3 months as compared with 7.8 months for the other patients (P = 0.004). Conclusions: Cetuximab pharmacokinetics in colorectal cancer patients can be described using a model combining linear and nonlinear elimination rates. PFS is influenced by global clearance of cetuximab, a parameter that can be estimated using cetuximab residual concentration on day 14. Clin Cancer Res; 17(19); 6329–37. ©2011 AACR.

URL de la notice	http://okina.univ-angers.fr/publications/ua9167 [12]
DOI	10.1158/1078-0432.CCR-11-1081 [13]
Lien vers le document	http://dx.doi.org/10.1158/1078-0432.CCR-11-1081 [13]
Titre abrégé	Clin Cancer Res

Liens
[1] http://okina.univ-angers.fr/publications?f[author]=16266
[2] http://okina.univ-angers.fr/publications?f[author]=16267
[3] http://okina.univ-angers.fr/publications?f[author]=16268
[4] http://okina.univ-angers.fr/publications?f[author]=800
[5] http://okina.univ-angers.fr/publications?f[author]=16270
[6] http://okina.univ-angers.fr/alain.morel/publications
[7] http://okina.univ-angers.fr/publications?f[author]=16271
[8] http://okina.univ-angers.fr/publications?f[author]=16272
[9] http://okina.univ-angers.fr/publications?f[author]=16273
[10] http://okina.univ-angers.fr/publications?f[author]=16170
[11] http://okina.univ-angers.fr/publications?f[author]=16274
[12] http://okina.univ-angers.fr/publications/ua9167
[13] http://dx.doi.org/10.1158/1078-0432.CCR-11-1081