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FEBS Open Bio. 2020 Jan 28.;


Abstract

Epstein-Barr virus (EBV)-associated gastric cancer (EBVaGC), whose prognosis remains controversial, is diagnosed by in situ hybridization of EBV-derived EBER1/2 small RNAs. In the Cancer Genome Atlas (TCGA)-Stomach Adenocarcinoma (STAD) project, the EBV molecular subtype was determined through a combination of multiple next-generation sequencing methods, but not by the gold standard in situ hybridization method. This leaves unanswered questions regarding the discordance of EBV positivity detected by different approaches and the threshold of sequencing reads. Therefore, we re-analyzed the TCGA-STAD RNA-seq dataset including 375 tumor and 32 normal samples, using our analysis pipeline. We defined a reliable threshold for EBV-derived next-generation sequencing reads by mapping them to the EBV genome with three different random arbitrary alignments. We analyzed the prognostic impact of EBV status on the histopathological subtypes of gastric cancer. EBV-positive cases identified by re-analysis comprised nearly half of the cases (49.6%) independent from infiltrating lymphocyte signatures, and showed significantly longer overall survival for adenocarcinomas of the “not otherwise specified” (NOS) type [P = 0.016 (log-rank test); HR 0.476; 95% CI 0.260–0.870, P = 0.016 (Cox univariate analysis)], but shorter overall survival for the tubular adenocarcinoma type [P = 0.005 (log-rank test); HR 3.329; 95% CI 1.406–7.885, P = 0.006 (Cox univariate analysis)]. These results demonstrate that the EBV-positivity rates were higher when determined by RNA-seq than when determined by EBER1/2 in situ hybridization. The RNA-seq-based EBV-positivity demonstrated distinct results for gastric cancer prognosis depending on the histopathological subtype, suggesting its potential to be used in clinical prognoses.

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Advances in colon-targeted nano-drug delivery systems: challenges and solutions.

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Advances in colon-targeted nano-drug delivery systems: challenges and solutions.

Arch Pharm Res. 2020 Jan 27.;

Authors: Naeem M, Awan UA, Subhan F, Cao J, Hlaing SP, Lee J, Im E, Jung Y, Yoo JW

Abstract

Nano-drug delivery systems (NDDS) for colon-targeted drug delivery are an active area of research on local diseases affecting the colon, such as ulcerative colitis, Crohn’s disease, colon cancer, and for the delivery of peptide or protein drugs and vaccinations. In particular, targeted nano-drug delivery to the colon is advantageous for colon-specific diseases because nanoparticles can accumulate in diseased parts, improve the efficacies of therapeutics, and enable localized treatments, which reduces systemic toxicity. However, there are many hurdles, such as burst drug release, enzyme and acidic degradation of drug and carrier in the stomach, pH variations, mucus entrapment, and systemic uptake in the upper small intestine, which could challenge and compromise the successful delivery of NDDS to the colon. With advancements in NDDS, it may be possible to overcome these challenges leading to efficient drug delivery for colon-specific disorders. This review describes a few of the potential colon-specific drug delivery areas and the challenges faced by colon-targeted orally administered delivery systems, and provides an updated summary of recent advances in the development of orally administered NDDS for colon targeting, and the future advances in this research.

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Gastric Xanthoma in the Pediatric Population: A Possible Herald for Malignancy?

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Gastric Xanthoma in the Pediatric Population: A Possible Herald for Malignancy?

A multicentre, phase IIa study of zolbetuximab as a single agent in patients with recurrent or refractory advanced adenocarcinoma of the stomach or lower oesophagus: the MONO study.

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A multicentre, phase IIa study of zolbetuximab as a single agent in patients with recurrent or refractory advanced adenocarcinoma of the stomach or lower oesophagus: the MONO study.


Abstract

BACKGROUND: Claudin 18.2 (CLDN18.2) is physiologically confined to gastric mucosa tight junctions; however, upon malignant transformation, perturbations in cell polarity lead to CLDN18.2 epitopes being exposed on the cancer cell surface. The first-in-class monoclonal antibody, zolbetuximab (formerly known as IMAB362), binds to CLDN18.2 and can induce immune-mediated lysis of CLDN18.2-positive cells.

PATIENTS AND METHODS: Patients with advanced gastric, gastro-oesophageal junction (GEJ) or oesophageal adenocarcinomas with moderate-to-strong CLDN18.2 expression in ≥50% of tumour cells received zolbetuximab intravenously every 2 weeks for five planned infusions. At least three patients were enrolled in two sequential cohorts (cohort 1300 mg/m²; cohort 2600 mg/m²); additional patients were enrolled into a dose-expansion cohort (cohort 3600 mg/m²). The primary end point was the objective response rate [ORR: complete and partial response (PR)]; secondary end points included clinical benefit (ORR+stable disease (SD)), progression-free survival, safety/tolerability, and zolbetuximab pharmacokinetic profile.

RESULTS: From September 2010 to September 2012, 54 patients were enrolled (cohort 1, n = 4; cohort 2, n = 6; cohort 3, n = 44). Three patients in cohort 1 and 25 patients in cohorts 2/3 received at least 5 infusions. Antitumour activity data were available for 43 patients, of whom 4 achieved PR (ORR 9%) and 6 (14%) had SD for a clinical benefit rate of 23%. In a subgroup of patients with moderate-to-high CLDN18.2 expression in ≥70% of tumour cells, ORR was 14% (n = 4/29). Treatment-related adverse events occurred in 81.5% (n = 44/54) patients; nausea (61%), vomiting (50%), and fatigue (22%) were the most frequent.
CONCLUSIONS: Zolbetuximab monotherapy was well tolerated and exhibited antitumour activity in patients with CLDN18.2-positive advanced gastric or GEJ adenocarcinomas, with response rates similar to those reported for single-agent targeted agents in gastric/GEJ cancer trials. CLINICALTRIALS. GOV NUMBER: NCT01197885.

PMID: 31987404 [PubMed — in process]

[Effect of STIL on the Gene Expression Profile of Gastric Cancer Cells].

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[Effect of STIL on the Gene Expression Profile of Gastric Cancer Cells].
Authors: Wang J, Dou XZ, Wang QY, Jiang WH, Yuan WH

Abstract
Objective To explore the molecular mechanism underlying gastric carcinogenesis and progression by using gene expression profiling array together with bioinformatics. Methods Lentivirus short hairpin RNA targeting STIL(ShSTIL)and scrambled sequence RNA(ShCon)were transduced into the gastric cancer cell line SGC-7901. RNA extraction, complementary DNA synthesis, construction of biotin-labelled amplified RNA probes, and hybridization with gene expression profile were consecutively performed. We collected corresponding data and analyzed differentially expressing genes(DEGs), followed by the analysis of gene ontology(GO) and Kyoto encyclopedia of genes and genomes(KEGG) enrichment, transcription factor regulating network, and protein-protein interacting networks. Results Compared with ShCon, a total of 417 and 87 genes were respectively down-regulated and up-regulated, respectively, in the ShSTIL group(P1 or

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[Analysis of Prognosis according to Type of Health Insurance in Five Major Gastrointestinal Cancer Patients in Public Hospitals: Single-institution Retrospective Study].

Authors: Lee DS, Lee J, Kim JW, Lee KL, Kim SH, Jung YJ

Abstract
Background/Aims: Public hospitals were established to provide high quality medical services to low socioeconomic status patients. This study examined the effects of public hospitals on the treatment and prognosis of patients with five-major gastrointestinal (GI) cancers (stomach cancer, colon cancer, liver cancer, bile duct cancer, and pancreatic cancer).
Methods: Among the 1,268 patients treated at Seoul National University Borameae Medical Center from January 2010 to December 2017, 164 (13%) were in the medicare group. The data were analyzed to identify and compare the clinical manifestations, treatment modality, and clinical outcomes between the groups.
Results: No statistically significant differences in the clinical data (age, sex), treatment method, and five-year survival rate were observed between the health insurance group and medicare group in the five major GI cancer patients. On the other hand, some medicare group patients tended more comorbidities and fewer treatment options than health insurance patients.
Conclusions: Public hospitals have a positive effect on the treatment and prognosis in medicare group patients with the five-major GI cancers.

PMID: 31986569 [PubMed — in process]