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Enteron

Dear Doctor,

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Medical Team, Micro Labs Ltd

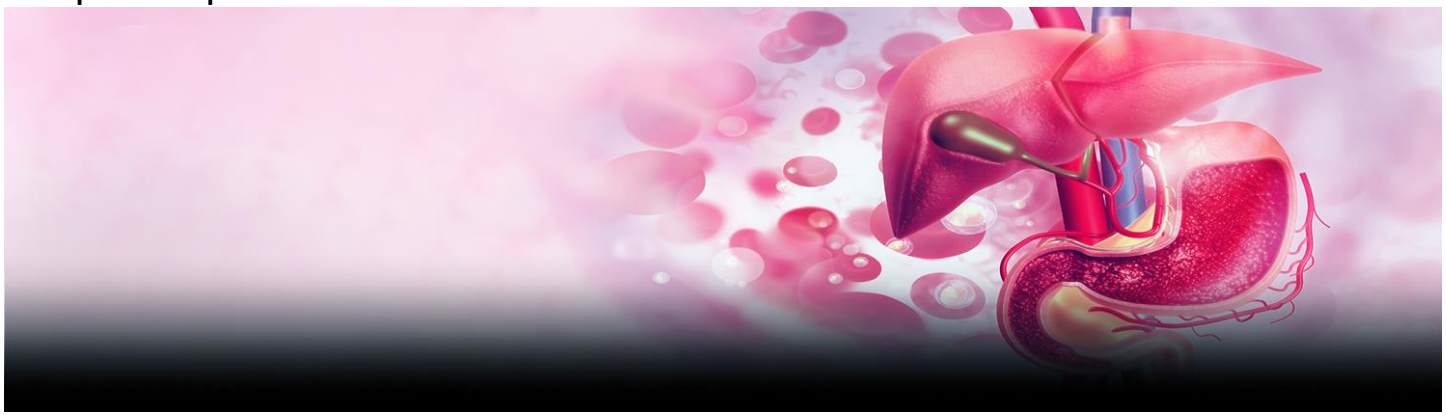
FDA Approves First-Line Immunotherapy in Liver Cancer

The FDA approved atezolizumab the PD-L1 immune checkpoint inhibitor for the first-line treatment of unresectable or metastatic liver cancer in combination with bevacizumab, a VEGF receptor inhibitor.

Approval was based on findings from IMbrave150, a Phase III study that randomized 501 hepatocellular carcinoma (HCC) patients 2:1 to either 1200 mg atezolizumab plus 15 mg / kg bevacizumab (intravenously administered every 3 weeks) or twice daily oral sorafenib, and showed improved survival outcomes and response rates with the combination. In a press release from Drugmaker Genentech, Richard Finn, MD, of the David Geffen School of Medicine at UCLA, said the results of the IMbrave150 study are truly transformative for patients with advanced liver cancer, one of the few cancers with rising death rates and limited first-line setting options. For the first time we have a regimen that significantly improves survival over sorafenib, the standard of care for first-line hepatocellular carcinoma since 2007, and provides patients with a favorable tolerability profile for improved disease controls.

Median overall survival in the immunotherapy-based combination group was not achieved compared with the kinase inhibitor sorafenib for 13.2 months (HR 0.58, 95 percent CI 0.42-0.79, P=0.0006), as was median progression-free survival (6.8 vs. 4.3 months, respectively; HR 0.59, 95 percent CI 0.47-0.76, P<0.0001). In 28 percent of patients in the combination arm, objective response levels for RECIST 1.1 were registered compared to 12 percent in the sorafenib arm. Through mRECIST, reaction levels were 33% vs. 13%, respectively (for both, P<0.0001). Hypertension (29.8 per cent), fatigue (20.4 per cent), and proteinuria (20.1 per cent) were common adverse events (AEs) with the combination. The incidence of grade 3/4 AEs between the two arms was similar, although severe AEs were slightly more common with atezolizumab-bevacizumab (38.0 percent vs. 30.8 percent) and included gastrointestinal bleeding, infections, and fever.

Source: U.S Food & Drug administration. 2020. Available at https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma. Accessed on 03-06-2020



A Large Cross-Sectional Study to evaluate the association Between H Pylori Infection and Short-segment/Long-segment Barrett's Esophagus

INTRODUCTION

Patients are predisposed to esophageal adenocarcinoma (EAC), a high-mortality disorder, by Barrett's esophagus (BE). Older age, male sex, white race, obesity, smoking use, hiatal hernia and gastroesophageal reflux disorder (GERD) have been reported as other risk factors for BE development in the past. Though infection with Helicobacter pylori (H pylori) has typically been considered a protective factor against BE, the relationship between H pylori and BE remains contentious. Case-control studies in western countries have reported an inverse association between H. Pylori-infection, and BE. As well, a meta-analysis revealed an inverse association.

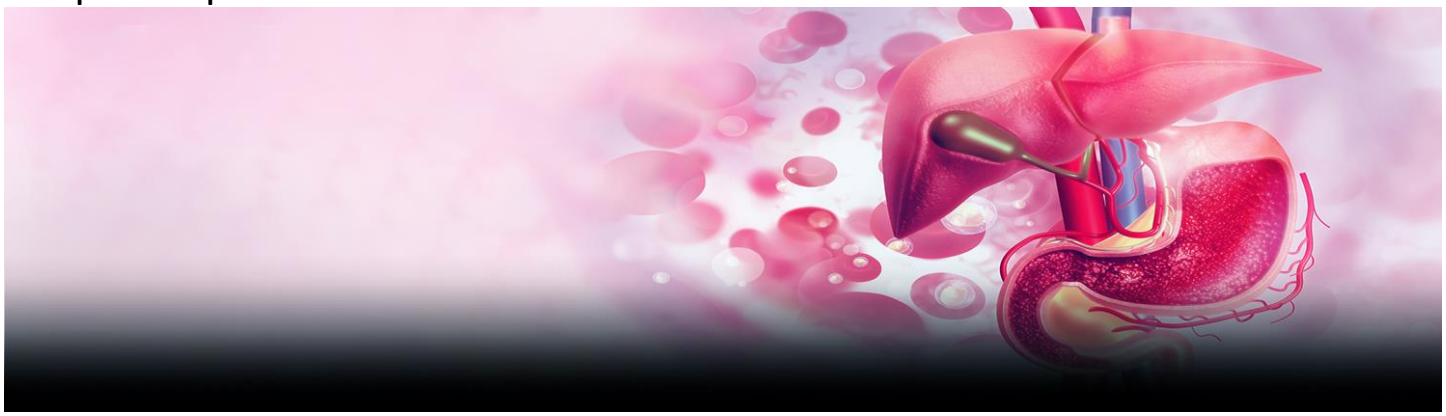
The association between H pylori infection and BE, by comparison, has been documented to be correlated with BE differently in different regions. The effect of segment duration BE on the relationship between infection with BE and H pylori has been barely examined. BE is classified into Barrett 's short-sectioned and long-sectioned esophagus (SSBE and LSBE) according to the segment lengths of the oesophageal mucosa with columnar metaplasia (minimum duration < 3 and roughly 3 cm, respectively). Subjects with SSBE have apparently slightly lower EAC production levels than those with LSBE. To date, only a few studies have carried out subgroup analyses of the relationship between H pylori infection and the various lengths of BE fragment. Such findings were heterogeneous in various regions and racial groups, too. In this cross-sectional analysis, it was intended to use a broad database of stable Japanese participants to examine the association between H pylori infection and the prevalence of SSBE / LSBE.

METHODS

The study subjects were 41,065 asymptomatic Japanese individuals who took medical surveys between October 2010 and September 2017. Using this large database of healthy Japanese subjects, they investigated the association between H. pylori infection and SSBE/LSBE. They used multivariable logistic regression analysis to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS

Among the study subjects, 36,615 were eligible for the analysis. H. pylori seropositivity was significantly associated with a lower rate of LSBE (OR: 0.42; 95% CI: 0.16-0.91) and a higher rate of SSBE (OR: 1.66; 95% CI: 1.56-1.78) after multivariate adjustment. In the subgroup analysis, H. pylori seropositivity was significantly associated with a high rate of SSBE in subjects without reflux esophagitis (RE) (OR: 1.73; 95% CI: 1.61-1.85). However, H. pylori seropositivity was not associated with SSBE in subjects with RE (OR: 1.07; 95% CI: 0.84-1.37).



	SSBE			LSBE		
	OR (95% CI)		*P*	OR (95% CI)		*P*
Sex	1.57 (1.46-1.69)	(male vs. female)	<0.001	2.37 (1.14-5.55)	(male vs. female)	0.03
Age	1.17 (1.14-1.20)	(/10 y)	<0.001	2.36 (1.90-2.93)	(/10 y)	<0.001
BMI	0.97 (0.93-1.01)	(/5 kg/cm^2)	0.10	—		—
HH	1.60 (1.50-1.72)		<0.001	4.17 (2.52-6.84)		<0.001
Smoking habit	1.03 (1.02-1.04)	(/5 pack-years)	<0.001	—		—
Alcohol drinking						
Nondrinker (<40 g/wk)	1 (reference)			1 (reference)		
Mild drinker (40-140 g/wk)	1.08 (1.01-1.15)		0.03	1.09 (0.55-2.12)		0.80
Moderate drinker (140-280 g/wk)	1.14 (1.06-1.23)		<0.001	1.64 (0.85-3.13)		0.13
Heavy drinker (>280 g/wk)	1.06 (0.97-1.15)		0.19	1.59 (0.79-3.15)		0.18
H. pylori seropositivity	1.66 (1.56-1.78)		<0.001	0.42 (0.16-0.91)		0.045
RE	1.70 (1.57-1.82)		<0.001	1.66 (0.94-2.85)		0.07

Some variables were excluded from the model by the backward elimination procedure with $P=0.2$.
BMI indicates body mass index; CI, confidence interval; HH, hiatal hernia; *H. pylori, Helicobacter pylori*; LSBE, long-segment Barrett's esophagus; OR, odds ratio; RE, reflux esophagitis; SSBE, short-segment Barrett's esophagus.

Predictors of SSBE and LSBE (Multiple Logistic Regression Analysis)

CONCLUSION

It was found that H pylori infection was significantly associated with SSBE. In addition, H pylori infection was significantly associated with SSBE in subjects without reflux esophagitis but not with SSBE in subjects with reflux esophagitis.

REFERENCE

Usui G, Sato H, Shinozaki T, et al. Association Between Helicobacter pylori Infection and Short-segment/Long-segment Barrett's Esophagus in a Japanese Population: A Large Cross-Sectional Study. J Clin Gastroenterol. 2020;54(5):439-444.

Relationship of the severity of Gastroperesis with Gastric Emptying, and Esophageal Function Testing

INTRODUCTION

Gastroparesis (Gastroperesis), a condition without functional interference with impaired gastric emptying, affects around 2 per cent of the adult population. Patients with gastroperesis can suffer a number of gastrointestinal (GI) symptoms including nausea, vomiting, early satiety, postprandial fullness and abdominal pain. There is a low link between traditional Gastroperesis signs and gastric emptying clinical testing — thus, the occurrence of these signs does not reflect the underlying pathophysiology. In addition to the normal signs of Gastroperesis, Gastroperesis patients may often suffer effects of GE reflux in the mouth, such as heartburn, regurgitation and bitter taste. The relationship of gastroesophageal reflux disease (GERD) to Gastroperesis is complex and not well understood. Theoretically, delayed gastric emptying in Gastroperesis raises the amount of gastric contents, which may eventually induce regurgitation of stomach contents into the esophagus, possibly by inducing proximal distension of the stomach and reducing the pressure of the oesophageal sphincter (LES).

The primary aim of this study was to determine the relationship of the severity of Gastroperesis with the severity of reflux, looking both at symptoms and objective testing for Gastroperesis and GERD. Secondary aims of the study were to: (1) determine the prevalence of esophageal motility disorders in Gastroperesis patients with reflux symptoms using esophageal manometry testing; (2) determine the presence of anxiety, depression, and somatization in Gastroperesis patients with reflux symptoms undergoing ambulatory pH monitoring.

METHODS

Patients referred to the academic center with symptoms of Gastroperesis completed the Patient Assessment of Upper Gastrointestinal Symptoms, Hospital Anxiety and Depression Scale, and Patient Health Questionnaire (PHQ)-15. They underwent 4-hour gastric emptying scintigraphy; and, if indicated, high-resolution esophageal manometry and esophageal pH impedance (EpHI).

RESULTS

Of 755 patients from July 2013 to May 2018, 432 had Gastroperesis with Gastroparesis Cardinal Symptom Index (GCSI) total score of 3.2 ± 0.1 (mean ± SEM) and heartburn/regurgitation subscore of 2.0 ± 0.1. A fourth (27.1%) of all Gastroperesis patients had moderate to very severe heartburn/regurgitation symptoms. Heartburn/regurgitation subscore had strong correlation with GSCI total score ($r=0.56$, $P< 0.01$), and weak correlation with 4-hour gastric retention ($r=0.11$, $P=0.02$). In total, 103 Gastroperesis patients underwent EpHI monitoring; time esophageal $pH< 4$ had no correlation with heartburn/regurgitation subscore. Less than half (41.7%) of the patients undergoing EpHI had gastroesophageal reflux disease by EpHI.

Gastroperesis patients with gastroesophageal reflux disease had more severe 4-hour gastric retention, and more frequently had decreased lower esophageal sphincter resting pressure and esophageal motility disorders. Heartburn/regurgitation subscore had moderate correlation with somatic symptoms, and weak correlations with anxiety and depression.

GSCI Total Score, HB/Rg Subscale, Gastric Retention, and 24-Hour Esophageal pH Impedance	HADS-Depression	HADS-Anxiety	PHQ-12
GCSI total score	**$r=0.26$ $P<0.01$**	**$r=0.26$ $P<0.01$**	**$r=0.36$ $P<0.01$**
HB/Rg subscale	**$r=0.22$ $P<0.01$**	**$r=0.26$ $P<0.01$**	**$r=0.43$ $P<0.01$**
GES: Retention at 2 h (normal ≤60%)	$r=0.10$ $P=0.05$	$r=-0.01$ $P=0.94$	$r=0.09$ $P=0.06$
GES: Retention at 4 h (normal ≤10%)	$r=-0.01$ $P=0.90$	$r=-0.06$ $P=0.19$	$r=-0.01$ $P=0.89$
% time pH < 4	$r=0.13$ $P=0.21$	$r=0.09$ $P=0.37$	$r=-0.05$ $P=0.61$
All reflux	$r=0.11$ $P=0.30$	$r=0.14$ $P=0.21$	$r=-0.01$ $P=0.92$
Nonacid reflux	$r=0.03$ $P=0.77$	$r=0.21$ $P=0.06$	$r=0.04$ $P=0.74$
Weakly acid reflux	$r=0.09$ $P=0.40$	$r=0.11$ $P=0.30$	$r=-0.01$ $P=0.96$
Acid reflux	$r=0.18$ $P=0.11$	$r=0.05$ $P=0.63$	$r=0.05$ $P=0.67$

Values in bold are statistically significant.
GCSI indicates Gastroparesis Cardinal Symptom Index; GES, gastric emptying scintigraphy; HADS, Hospital Anxiety and Depression Scale; HB, heartburn; PHQ, Patient Health Questionnaire; Rg, regurgitation.

Correlation of HADS-Anxiety, HADS-Depression, and PHQ-12 Scores to GSCI Total Score, HB/Rg Subscale, Gastric Retention, and 24-Hour Esophageal pH Impedance Results in Gastroparesis Patients

CONCLUSION

A fourth of patients with Gastroperesis develop mild to extremely extreme reflux symptoms, including regular usage of antireflux drugs. Such reflux effects associate mildly to significantly with the intensity of standard Gastroperesis effects, although weakly with gastric retention for four hours. Reflux effects of patients with Gastroperesis are negatively associated with objective reflux tests, similar to the preceding literature indicating low association between effects of Gastroperesis and accurate assessments of gastric emptying. Gastroperesis patients with signs of reflux may suffer concomitant disturbances of the esophageal motility. Assessing the extent of reflux in patients with Gastroperesis, both symptomatically and probably clinically, could be critical for treating their symptoms effectively.

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