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RESPONSE TO REVIEWERS

Thank you for the opportunity to revise our work. We appreciate the time the reviews took to critically examine our manuscript. Our response to their individual reviews can be found following their comments in red.

We have taken this opportunity to update our manuscript and include two studies that were referenced and have had final results published during the review period. Below we have listed all of the changes that were made to the manuscript. The changes are highlighted within the revised manuscript document.

Page 1:

Manuscript No was added.

“Manuscript NO: 46298”

Open-Access statement was added.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>



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Page 3:

The Author(s) statement was added.

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Page 8:

Outcomes of the recently published KLASS-02 trial were included as this trial was previously described as ongoing.

Fewer studies have addressed laparoscopy in advanced gastric cancer. The KLASS-02 trial randomized patients with locally advanced gastric cancer to either laparoscopic or open distal gastrectomy^[40]. Short term outcomes from this trial were recently published and demonstrated benefits in terms of lower complication rates, lower pain score, earlier return of bowel function, and shorter hospital length of stays compared to open surgery^[41].

Page 10:

Outcomes of the recently published FLOT4 trial were included as this trial was previously described as ongoing.

Recent phase III results of the FLOT4 randomized trial showed improved median OS of 50 months for patient receiving the FLOT regimen compared to 35 months for those on ECF/ECX with similar toxicities between the two groups^[55].

Page 12:

The following phrase was added to better describe the patient population who were suggested to benefit from chemoradiation:

Similarly, the ARTIST trial, which was designed to compare adjuvant chemotherapy to chemoradiation, failed to demonstrate a difference in disease-free and overall survival; however, subgroup analysis suggested that patients with intestinal type histology and lymph node metastasis, in particular, may benefit from chemoradiation^[63].

Page 21:

The reference for the KLASS-02 trial was added.

41 **Lee HJ**, Hyung WJ, Yang HK, Sang UH, Park YK, An JY, Kim W, Kim HI, Kim HH, Ryu SW, Hur H, Kong SH, Cho GS, Kim JJ, Park DJ, Ryu KW, Kim YW, Kim JW, Lee JH, Kim MC. Short-term Outcomes of a Multicenter Randomized Controlled Trial Comparing Laparoscopic Distal Gastrectomy with D2 Lymphadenectomy to Open Distal Gastrectomy for Locally Advanced Gastric Cancer (KLASS-02-RCT). *Ann Surg* 2019; 1-9. [PMID: 30829698 DOI: 10.1097/SLA.0000000000003217]

Page 24:

The reference for the FLOT4 trial was added.

55 **Al-Batran SE**, Homann N, Pauligk C, Goetze TO, Meiler J, Kasper S, Kopp HG, Mayer F, Haag GM, Luley K, Lindig U, Schmiegel W, Pohl M, Stoehlmacher J, Folprecht G, Probst S, Prasnikar N, Fischbach W, Mahlberg R, Trojan J, Koenigsmann M, Martens UM, Thuss-Patience P, Egger M, Block A, Heinemann V, Illerhaus G, Moehler M, Schenk M, Kullmann F, Behringer DM, Heike M, Pink D, Teschendorf C, Lohr C, Bernhard H, Schuch G, Rethwisch V, von Weikersthal LF, Hartmann JT, Kneba M, Daum S, Schulmann K, Weniger J, Belle S, Gaiser T, Oduncu FS, Guntner M, Hozaeel W, Reichart A, Jäger E, Kraus T, Mönig S, Bechstein WO, Schuler M, Schmalenberg H, Hofheinz RD; FLOT4-AIO Investigators. Perioperative

Chemotherapy with Fluorouracil plus Leucovorin, Oxaliplatin, and Docetaxel versus Fluorouracil or Capecitabine plus Cisplatin and Epirubicin for Locally Advanced, Resectable Gastric or Gastro-oesophageal Junction Adenocarcinoma (FLOT4): a Randomised, Phase 2/3 Trial. *Lancet* 2019; **393**: 1948-1957. [PMID: 30982686 DOI: 10.1016/S0140-6736(18)32557-1]

Page 31:

The information on the KLASS-02 Trial in Table 1 was updated and abbreviations were identified below the table.

KLASS-02**	Korea	Complete	2011-2015	Randomization to open or laparoscopic gastrectomy and D2 lymph node resection	Decreased complication rates and pain scores with shorter hospital stays in laparoscopic resections
JCOG 0703*	Japan	Complete	2007-2008	Prospective study with patients undergoing laparoscopic distal gastrectomy with D1 lymph node resection	Laparoscopic surgery was safe with lower than expected rates of anastomotic leaks and pancreatic fistulas

* Clinical stage I gastric cancers only

**Locally advanced gastric cancers only

Dutch Gastric Cancer Group Trial (DGCT), Italian Gastric Cancer Study Group (IGCSG), year (yr), lymph node (LN), Korean Laparoscopic Surgical Society (KLASS), Japan Clinical Oncology Group (JCOG)

Page 32:

The information on the FLOT4 Trial in Table 2 was updated and abbreviations were identified below the table.

AIO-FLOT4 (Phase III)	Germany	Complete	2010- 2015	Neoadjuvant ECF/ECX	Epirubicin and cisplatin with either 5-FU (ECF) or capecitabine (ECX)	Improved OS in FLOT group with no increase in toxicities
				Neoadjuvant FLOT	Docetaxel, oxaliplatin, 5-FU with leucovorin	

Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC), United Kingdom (UK), 5-fluorouracil (5-FU), progression-free survival (PFS), overall survival (OS), disease-free survival (DFS)

Page 34:

Abbreviations were identified below Table 3.

TOPGEAR ACTRN12609000035224	Australia	Ongoing	-	Perioperative chemo with Neoadjuvant CRT	Perioperative chemo Epirubicin, cisplatin, 5-FU (ECF) Chemo: epirubicin, cisplatin, 5-FU (ECF) CRT: 45 Gy with 5-FU	-
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Intergroup (INT), United States (US), chemoradiation therapy (CRT), gray (Gy), disease-free survival (DFS), overall survival (OS), month (m), 5-fluorouracil (5-FU), ChemoRadiotherapy after induction chemotherapy in Cancer of the Stomach (CRITICS), chemotherapy (chemo), lymph node (LN), Trial Of Preoperative therapy for Gastric and Esophago-gastric junction Adenocarcinoma (TOPGEAR)

Page 36:

Abbreviations were identified below Table 4.

GASTRICHIP NCT01882933	Multiple	Ongoing	-	HIPEC	Curative gastrectomy with D1-D2 lymph node dissection Curative gastrectomy with D1-D2 lymph node dissection with HIPEC	IP Oxaliplatin with IV 5-FU and leucovorin	-
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Endothelial growth factor receptor (EGFR), chemotherapy (chemo), progression-free survival (PFS), overall survival (OS), Avastin in Gastric Cancer (AVAGAST), vascular endothelial growth factor receptor (VEGFR), months (m), Trastuzumab for Gastric Cancer (ToGA), human epidermal growth factor receptor 2 (HER2), 5-fluorouracil (5-FU), programmed death-ligand 1 (PD-L1), hyperthermic intraperitoneal chemotherapy (HIPEC), intraperitoneal (IP), intravascular (IV)



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46298

Title: Advancements and Challenges in Treating Advanced Gastric Cancer in the West

Reviewer's code: 02731983

Reviewer's country: Turkey

Science editor: Ying Dou

Reviewer accepted review: 2019-02-19 23:16

Reviewer performed review: 2019-02-19 23:37

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review is fair enough for the reader to understand the recent advancements in gastric cancer management.



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RESPONSE TO REVIEW

Thank you for your review.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46298

Title: Advancements and Challenges in Treating Advanced Gastric Cancer in the West

Reviewer's code: 00001114

Reviewer's country: Japan

Science editor: Ying Dou

Reviewer accepted review: 2019-04-08 05:51

Reviewer performed review: 2019-04-13 03:24

Review time: 4 Days and 21 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review entitles "Advancements and Challenges in Treating Advanced Gastric Cancer in the West" is a well-written and comprehensive review of the current state in treating advanced gastric cancer in the West. I have no specific comment. Thank you.



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1 Title. Adequate 2 Abstract. Yes 3 Keywords. Yes 4 Background. Yes 5 Methods. Not applicable 6 Results. Not applicable 7 Discussion. Yes 8 Illustrations and tables. Yes 9 Biostatistics. Not applicable 10 Units. Not applicable 11 References. Yes 12 Quality of manuscript organization and presentation. Good 13 Research methods and reporting. Not applicable 14 Ethics statements. Not applicable

RESPONSE TO REVIEW

Thank you for taking the time to review our manuscript.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46298

Title: Advancements and Challenges in Treating Advanced Gastric Cancer in the West

Reviewer’s code: 02531403

Reviewer’s country: Italy

Science editor: Ying Dou

Reviewer accepted review: 2019-04-19 11:24

Reviewer performed review: 2019-04-19 13:38

Review time: 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I read with interests the manuscript 46298 about the Advancements and Challenges in Treating Advanced Gastric Cancer in the West. I would to highlight the importance of the research and the significance of the research findings, with regards to the



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Advancements and Challenges in Treating Advanced Gastric Cancer in the West. The quality of the manuscript's presentation and readability is high.

The main and short titles accurately reflect the major topic and content of the study.

The abstract provides a clear delineation between the research background, objectives, materials and methods, results (including important data), and conclusions. The abstract present the innovative and significant points related to the background, objectives, materials and methods, results (including important data), and conclusions.

Introduction: the introduction is well described.

Materials and Methods: **please clarify if this is a systematic or a narrative review.**

Results: N/A

Discussion: The section is well organized. The conclusions drawn are appropriately supported by the literature. The section describes findings based upon systematic theoretical analyses of the results and provide valuable conclusions.

References: The references are appropriate, relevant, and up-to-date

Tables and Figures: The tables and figures reflect the major findings of the study. The tables and figures are designed to present the maximal amount of information in the most concise and clear manner

RESPONSE TO REVIEW

Thank you for taking the time to critically review our manuscript.

This review is a narrative review describing the progressions and difficulties in the treatment of gastric cancer in the West. This is not a full systematic review.