# Clinical progress in inoperable or recurrent advanced gastric cancer treatment from 1,004 single institute experiences between 2007 and 2018

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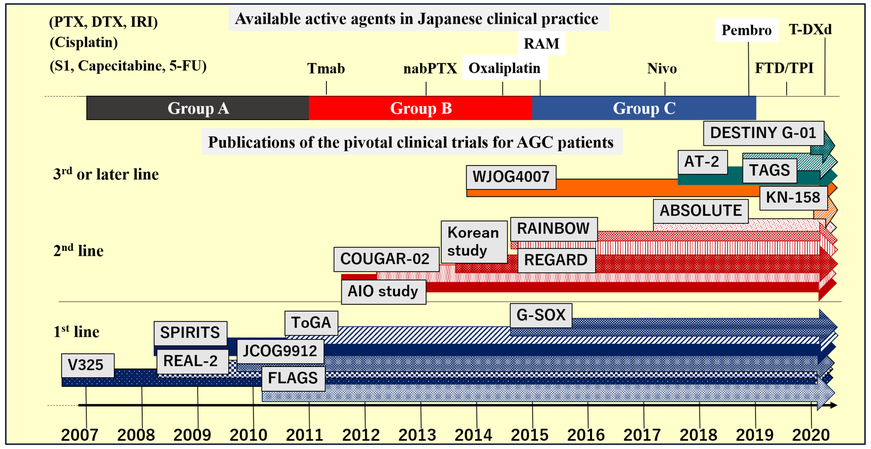
## BACKGROUND

- ✓ In the past decade, several successful clinical trials provided new therapeutic agents approved for clinical management of advanced gastric cancer (AGC). [1-18)]
- ✓ Currently, Japanese AGC patients could receive systemic chemotherapy at most in the fifth or sixth (if HER2-positive) line as standard treatment in the clinical practice.
- ✓ It is unknown whether these practice-changing results actually altered our dairy practice.

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## AIM

- ✓ This study was conducted to elucidate how successful clinical trials have influenced clinical practice for the future development of clinical trials in this field.

## METHODS

- ✓ We retrospectively reviewed medical records of AGC patients who received between 2007 and 2018 and divided them into three groups: Groups A, B, and C: 2007–2010, 2011–14, and 2015–18, respectively.
- ✓ We compared the clinicopathological features, treatment details, and clinical outcomes between the three groups.
- ✓ Main inclusion criteria were the following criteria: (1) had histologically proven advanced esophagogastric junction (EGJ) and stomach adenocarcinoma; (2) received combination chemotherapy containing fluoropyrimidine and platinum; (3) received no prior systemic chemotherapy for metastasis; and (4) provided written informed consent for receiving the treatment.
- ✓ We excluded patients with other types of advanced tumors and those with early recurrence (<6 months after the final administration of neoadjuvant or adjuvant chemotherapy).

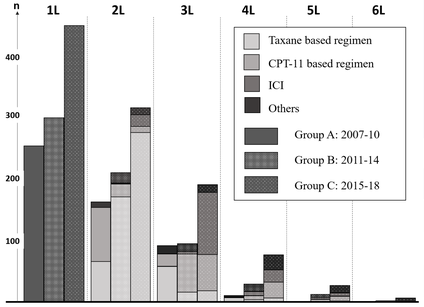
## DISCLOSURE

The authors declare no conflicts of interest associated with this presentation.

**Table 1. Patient's characteristics (N =1,004)**

| n (%) | Group A n=254 (%) | Group B n=300 (%) | Group C n=450 (%) | *P-value* |
|---|---|---|---|---|
| **Age median (range)** | 61 (16-78) | 62 (30-82) | 66 (21-84) | |
| Age<75 / ≥75 | 249 (98)/5 (2) | 286 (95)/14 (5) | 408 (91)/42 (9) | <0.001 |
| **Sex** | | | | |
| Male / Female | 179 (71)/75 (30) | 185 (62)/115 (38) | 292 (65)/158 (35) | 0.092 |
| **ECOG PS** | | | | |
| 0 / ≥1 | 218 (88)/30 (12) | 200 (67)/98 (33) | 258 (57)/192 (43) | <0.001 |
| **Lauren Classification** | | | | |
| Intestinal / Diffuse | 100 (39)/153 (60) | 200 (67)/98 (33) | 155 (34)/295 (66) | 0.461 |
| **Location** | | | | |
| EGJ or Cardia / Stomach | 36 (14)/216 (85) | 56 (19)/234 (78) | 102 (22)/342 (76) | 0.021 |
| **Extent of disease** | | | | |
| Metastatic / Recurrence | 224 (88)/8 (3) | 252 (84)/48 (16) | 360 (80)/90 (20) | <0.001 |
| **Prior Gastrectomy** | | | | |
| yes / no | 94 (37)/160 (63) | 108 (36)/192 (64) | 118 (26)/332 (74) | 0.002 |
| **No. of Metastases** | | | | |
| 2> / ≥2 | 175 (69)/79 (31) | 233 (78)/67 (22) | 291 (65)/159 (35) | <0.001 |
| **Fluoropyrimidine** | | | | |
| S1 / Capecitabine / 5-FU | 237 (93)/18 (7)/0 (0) | 217 (72)/80 (27)/3 (1) | 317 (70)/101 (22)/32 (7) | <0.001 |
| **Platinum** | | | | |
| Cisplatin / Oxaliplatin | 248 (98)/6 (2) | 261 (87)/29 (10) | 62 (14)/373 (83) | <0.001 |

**Figure 1. No. of subsequent therapies**



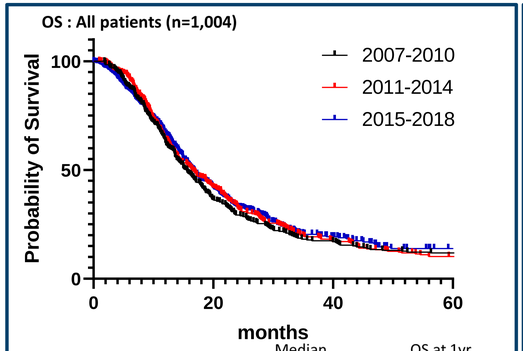

This bar graph shows the patient number (vertical axis) at each line of chemotherapy (horizontal axis) by study period. A total number of patients were increasing by age at any line of chemotherapy. Only limited number of patients received 3≥ line of chemotherapy. The preferentially chosen treatment regimens were different among study period in second and third-line treatment.

**Table 2. The proportions of subsequent therapies**

| | 1L/2L | 2L/3L | 3L/4L | 4L/5L |
|---|---|---|---|---|
| Group A | 72.7% | 55.2% | 11.6% | 0.0% |
| Group B | 77.2% | 47.5% | 30.1% | 42.9% |
| Group C | 81.9% | 66.4% | 42.6% | 37.7% |

## RESULTS

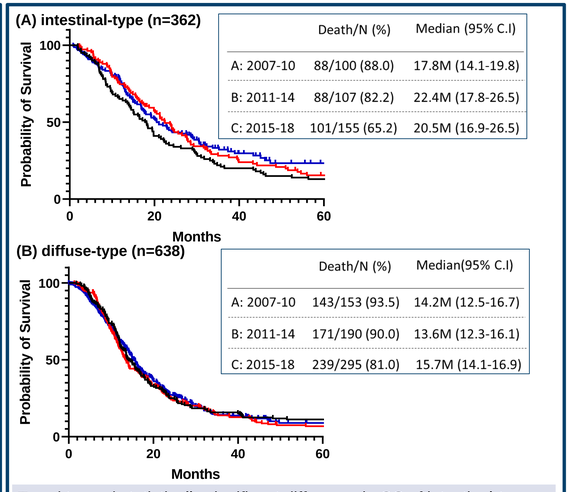
**Figure 2. Kaplan-Meier Curve of OS according to the study periods**




| | Death/N (%) | Median (95% CI) | OS at 1yr (95% CI) |
|---|---|---|---|
| A: 2007-2010 | 232/254 (91.3) | 15.5M (13.6-17.6) | 62.6% (56.3-68.2) |
| B: 2011-2014 | 260/300 (86.7) | 16.5M (14.1-19.0) | 64.0% (58.2-69.1) |
| C: 2015-2018 | 340/450 (75.6) | 16.8M (15.0-18.2) | 66.8% (62.1-71.0) |

There was no statistically significant difference both in OS and PFS of whole population between any two groups.

**Figure 3. Kaplan-Meier Curve of OS according to histological subtypes**

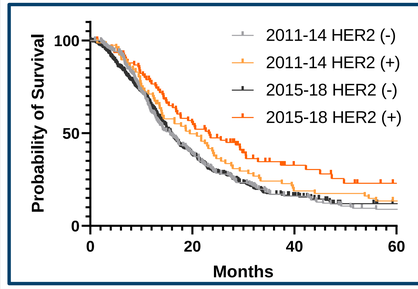



| | Death/N (%) | Median (95% C.I) |
|---|---|---|
| A: 2007-10 | 88/100 (88.0) | 17.8M (14.1-19.8) |
| B: 2011-14 | 88/107 (82.2) | 22.4M (17.8-26.5) |
| C: 2015-18 | 101/155 (65.2) | 20.5M (16.9-26.5) |

| | Death/N (%) | Median(95% C.I) |
|---|---|---|
| A: 2007-10 | 143/153 (93.5) | 14.2M (12.5-16.7) |
| B: 2011-14 | 171/190 (90.0) | 13.6M (12.3-16.1) |
| C: 2015-18 | 239/295 (81.0) | 15.7M (14.1-16.9) |

Trend toward statistically significant difference in OS of intestinal-type AGC was observed between Group A and Group B or C. However, Kaplan-Meier curves of OS of diffuse-type AGC were almost identical.

**Figure 4. Kaplan-Meier Curve of OS according to HER2 status (Group B and C)**




| | Death/N (%) | Median (95% C.I) | HR (95% C.I) | *P*-value |
|---|---|---|---|---|
| Group B: 2011-2014 | | | | |
| HER2 (-) | 189/217 (87.1) | 15.6M (13.2-18.2) | ref | 0.135 |
| HER2 (+) | 66/76 (86.8) | 19.5M (13.9-24.1) | **0.80 (0.60-1.06)** | |
| Group C: 2015-2018 | | | | |
| HER2 (-) | 274/352 (77.8) | 15.7M (14.2-17.3) | ref | **0.001** |
| HER2 (+) | 61/93 (65.6) | 23.2M (17.1-30.0) | **0.68 (0.51-0.90)** | |

The HR for mortality in HER2-positive AGC, compared to HER2-negative AGC, improved between groups B and C.

## DISCUSSIONS

- ✓ The increasing availability of chemotherapy options has expanded chemotherapeutic indications and caused the imbalance of patient characteristics between three groups.
- ✓ Second and later line Chemotherapy had been performed with high proportion of patients in the Group A. Thus, global establishment of second and later line therapy had a little impact on our dairy practice.
- ✓ Due to the shorter follow-up, the long-tail effect by immune therapy would not be adequately evaluated in this study. Updated analysis would be warranted.

## CONCLUSIONS

- ✓ Prolongation of survival was not observed in the overall study population in the past decade, but was clearly evident in HER2-positive AGC. The prognosis of diffuse-type AGC remains dismal.
- ✓ Further development of biomarker-driven therapy is warranted to improve the prognosis of AGC patients.