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STUDY PROTOCOL

PROTOCOL TITLE:
Development of a Clinical Decision Support System (CDSS) with Artificial Intelligence for Gastric and Esophageal Adenocarcinomas

PROTOCOL VERSION: 2.0
PROTOCOL DATE: 18 December 2020

PRINCIPAL INVESTIGATOR:
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STUDY SITE:
National University Hospital
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STUDY PROTOCOL

1. BACKGROUND AND RATIONALE

Management of cancer is a complex process which involves numerous specialists and stakeholders. In view of this, institutions worldwide have adopted the use of Multidisciplinary Team Meeting (MDTM) for decision of cancer care. By tapping on the collective specialized knowledge and experience of various specialties, MDTM have been shown to result in more accurate staging, more appropriate recommendations and improved patient outcomes [1-2]. At our institution, cancer cases are similarly discussed at regular MDTM which comprises surgeons, oncologists, pathologists and radiologists who review and recommend treatments.

However, in smaller centres or centres with limited resources, MDT is not available. In those clinics, cancer treatment will be relied on the responsible clinician. Delivery of timely and appropriate cancer care could be a challenge. Additionally, clinicians and specialists, with their busy schedule, is impossible to keep abreast of all the new developments in cancer research. With rapid advances in scientific research, this pool of knowledge is expected to continue to burgeon, making keeping up-to-date increasingly onerous.

To address this need, clinicians have adopted the use of Clinical Decision Support Systems (CDSSs) to augment clinical care and decision-making. These are platforms which aim to enhance medical decisions with targeted up-to-date knowledge, patient information, and other health information [3]. Various studies have shown CDSSs to be beneficial in selected settings such as patient safety and diagnosis [4], and to even increase adherence to clinical guidelines [5]. In recent years, advancements in artificial intelligence have also seen its use expand to include CDSSs for oncologic therapy selection, such as IBM's Watson for Oncology (WFO). In a 2018 study, WFO's ability to provide treatment advice for breast cancer was compared against recommendations from a multidisciplinary board, where it showed a high degree of concordance [6]. Since then, several other studies have sought to examine WFO's ability to provide treatment recommendations for cancer such as ovarian [7], gastric [7,8], lung [7,9-10], cervical [11] and colorectal [7] cancers, with mixed results. In particular, both studies which examined the recommendations for gastric cancers showed a much lower concordance rate compared to other cancers [7,8]. One reason for the discordance is that WFO was developed based on patient data and treatment recommendation from experts at at Memorial Sloan Kettering Cancer Center, USA. There is significant difference in practice and preference in various geographic regions and individual clinics.

In view of the above, we sought to develop an alternative CDSS for oncologic therapy selection through partnership with Ping An Health Technology, beginning with gastric and oesophageal adenocarcinoma. This would be done with the platform utilizing only major international guidelines from leading authorities such as NCCN, ESMO and JGCA together with high-quality published evidence from high impact medical journals to arrive at case-specific treatment recommendations. In addition, our CDSS system incorporate machine learning which can adapt the preference of individual clinics in different continents. This platform was developed jointly by the specialists from the MDT at National University Health System and National University Cancer Institute, Singapore together with the computing scientists from Ping An Health Technology. We would like to validate this system prospectively at this multicenter clinical trial

by comparing its recommendations with that from the MDT of different tertiary care institutions worldwide.

2. HYPOTHESIS AND OBJECTIVES

2.1. Hypothesis

The recommendations between a specialist-driven multidisciplinary tumour board and an artificial intelligence powered clinical decision support tool would be compared in this study. Its results could potentially improve outcomes for cancer care.

2.2. Primary Objectives

Comparative agreement in recommendations between the two study groups, as measured by concordance rate.

2.3. Secondary Objectives

To identify the reason for the discordance.

2.4. Potential Risks and benefits:

There is minimal risk to our patients as the treatment is still decided by the clinical team as per clinical practice. The comparison is made by our research staffs. The recommendation by Artificial Intelligence Multidisciplinary Tumour Board online platform (AIM online platform) is made available to the clinicians. The clinicians can refer it as an option for their consideration. The risk of the study is related to the data breach during data collection. However, this risk will be minimised by de-identifying using a unique code number and only the study team member will have access to the patient identification.

3. STUDY POPULATION

3.1. List the number of subjects to be enrolled.

We aim to include:

1. Discovery phase: 400 cases (only NUH and NTFGH)
2. Internal retrospective validation phase: 100 cases (only NUH and NTFGH)
3. Prospective validation phase: 1500 cases in a 2 to 3 years

3.2. Population (base)

All patients listed in tumour board with gastric cancer, oesophageal cancer and gastro-oesophageal junction carcinoma.

3.3. Inclusion Criteria

A. In discovery and internal retrospective validation part:
    a. Patients with primary gastric adenocarcinoma including preinvasive carcinoma or
    b. Patients with gastroesophageal junction cancers or

c. Patients with oesophageal cancer including adenocarcinoma, squamous cell carcinoma and preinvasive carcinoma subtypes.

B. In prospective validation part:
   a. Patients with primary gastric adenocarcinoma including preinvasive carcinoma or
   b. Patients with esophageal or gastroesophageal junction adenocarcinoma

3.4. Exclusion Criteria

A. In discovery and internal retrospective validation part:
   a. Patients with other primary cancers involving the stomach or oesophagus
   b. Patients with other cancer subtypes
   c. Patients with concomitant cancers of other organs

B. In prospective validation part:
   a. Patients with esophageal squamous cell carcinoma
   b. Patients who participate in clinical trials where the treatment modality is not standard of care

4. TRIAL SCHEDULE

Patients will not undergo any procedures for the study. This is an observational study only. Patients will be treated according to national guidelines. The treatment received by patients may differ per country.

5. STUDY DESIGN

Our study comprises three parts: The Discovery Part (Part 1), The Internal Retrospective Validation Part (Part 2) and The Prospective Validation Part (Part 3).

In the discovery part, de-identified retrospective data on patient and disease characteristics as well as our MDTM recommendations would be collected and utilized to develop the CDSS platform, named AIM online platform, with help from our collaborative partner, Ping An Technology (Shenzhen, China).

In the internal retrospective validation part, additional de-identified retrospective data different from the discovery part will be entered manually into AIM online platform by two trained clinicians, who would be blinded to the treatment recommendations given by the MDTM. These treatment recommendations for each patient would then be collated and compared to the MDTM recommendation. Concordance would be determined by whether the MDTM recommendation is listed in AIM's list of treatment recommendations as a) 1st Recommendation, b) 2nd Recommendation, c) 3rd Recommendation, or d) Not Concordance.

In the external validation part, prospective patient data would be collected over a period of 2 to 3 years from more than 10 different institutions, including centres from Europe, North America and Asia. The prospective data is defined as data collected after 1 May 2020, and the study team will only be collecting data from participants who have given their consent (this may differ per country as per local IRB's requirement). These patient data would be fed into the AIM online

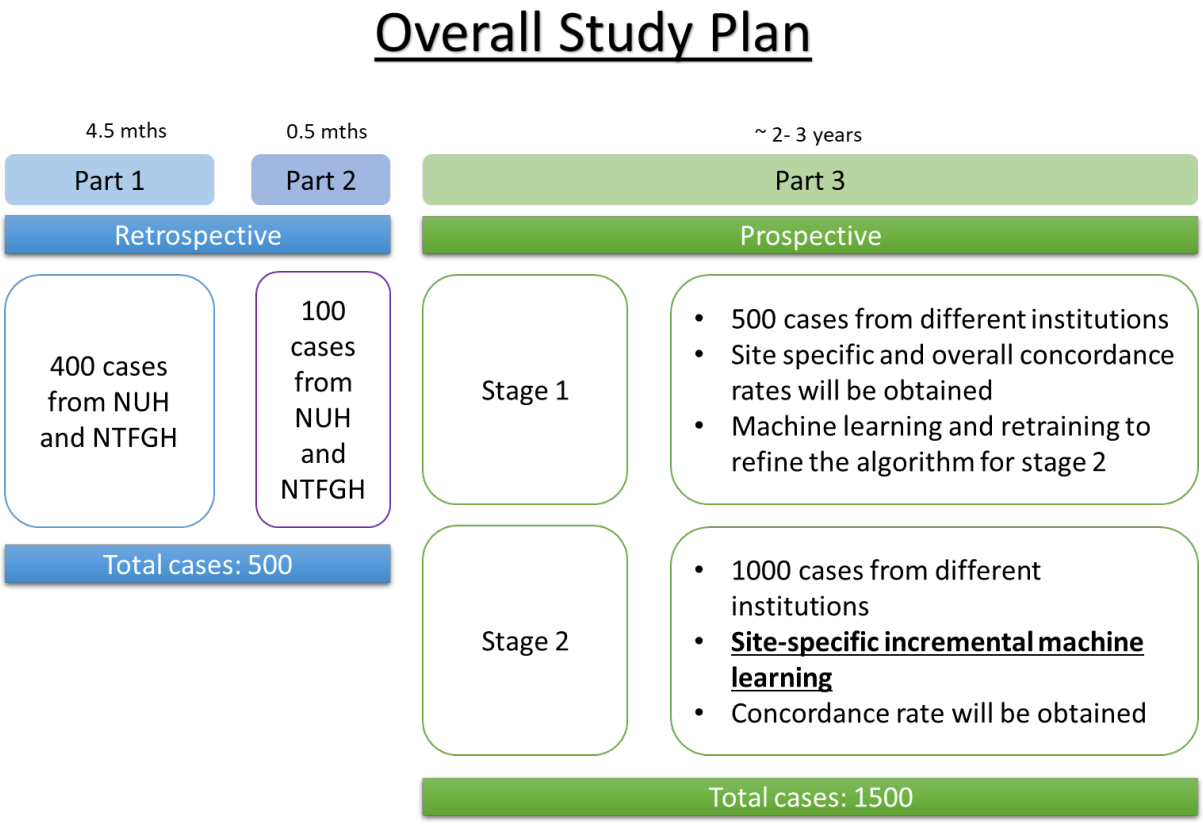
platform within one month of MDTM discussion at these institutions, with clinicians blinded to the generated recommendations. These recommendations would then be immediately compared to the MDTM recommendations to determine concordance. Concordance would be determined by whether the MDTM recommendation is listed in AIM's list of treatment recommendations as a) 1st Recommendation, b) 2nd Recommendation, c) 3rd Recommendation, or d) Not Concordance. All these data will be captured in the AIM platform.

There are 2 stages of validation in the external validation part. In Stage 1, 500 cases will be included from different institutions. The site specific and overall concordance rates will be obtained and analysed. The AIM model will be re-trained to refine the algorithm based on the data collected in stage 1. In Stage 2, 1000 cases will be included from different institutes and site-specific incremental machine learning will be activated. The concordance rate will be obtained and analysed.

At the end of the study, we will also analyse predictive factors for disagreement.

5.1. Summary of Study Design

This is a multinational observational cohort study. The duration of the study will approximately be 3.5 years (4.5 months for part 1, 0.5 months for part 2 and 2 to 3 years for part 3). Part 1 and 2 will be conducted in NUH and NTFGH only. Part 3 will be conducted in more than 10 different institutes, including centres from Europe, North America and Asia.



6. DATA ANALYSIS

6.1. Data Quality Assurance

All the data will be obtained from the tumour board list. The investigator will ensure the data entries are accurate and correct.

6.2. Data Entry and Storage

All the data will be handled confidentially and anonymously.

In part 1 and 2, the data will be entered into a password encrypted excel sheet and de-identified by a central third party. The individual-identifiers will be kept by the central third party.

In part 3, the anonymous data will be fed into the AIM online platform directly. Only registered user can feed the data into the AIM online platform. A subject identification code will be assigned to each patient and the subject code list is kept within the institution. Ping An team will be responsible for extracting the data for concordance analysis.

7. STATISTICAL ANALYSIS

Descriptive statistics for both the patient population as well as cancer characteristics would be calculated and tabulated in means and medians where appropriate.

Concordance would be calculated and presented as percentages.

8. ETHICAL CONSIDERATIONS

8.1. Regulation statement

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) GCP guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki. The investigator must ensure that the study is conducted in accordance with the provisions as stated in the ICH regulations and complies with prevailing local laws and customs.

8.2. Informed Consent

These procedures may differ per country. In general, prior collecting patient data, the investigator or his/her representative will explain the nature of the study to the subject and answer all questions regarding this study. Each informed consent will be reviewed, signed and dated by the subject and the person who administered the informed consent. A copy of each informed consent will be given to the subject and each original will be placed in the subject's medical record.

8.3. IRB review

Each participating institution must provide for the review and approval of this protocol and the

associated informed consent documents by the local IRB prior conducting any research activities.

Any amendments to the protocol will require local IRB approval prior to implementation of any changes made to the study design. All substantial amendments will be notified to the IRB and to the competent authority. Non-substantial amendments such as administrative changes will not be notified to the local IRB and the competent authority, but will be recorded and filed by the sponsor.

The sponsor/ investigator will submit a summary of the progress of the trial to the local IRB yearly.

The end of the study is defined as 100 valid cases has been recorded per institute. In case the study is ended prematurely, the investigator will notify the local IRB within 7 days, including the reasons for premature termination. Within 30 days after the end of the study, the investigator/ sponsor will submit a final study report with the results of the study, to the local IRB.

8.4. Confidentiality of Data and Patient Records

Information collected for this study will be kept confidential. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to the participating subjects. Patient records, to the extent of the applicable laws and regulations, will not be made publicly available. Data collected and entered into the AIM online platform are the property of NUH and Ping An. In the event of any publication regarding this study, patient's identity will remain confidential.

9. RETENTION OF TRIAL DOCUMENTS

Records for all participants, including CRFs, all source documentation (containing evidence to study eligibility, history and physical findings, laboratory data, results of consultations, etc.) as well as IRB records and other regulatory documentation should be retained by the PI in a secure storage facility for up to 6 years. The records should be accessible for inspection and copying by authorized authorities.

10. AUTHORSHIP

10.1. Writing committee on behalf of the study group

Centers providing at least 50 cases will be eligible for 1 authorship position within the writing committee, with eligibility for 2 authorship positions when providing at least 100 cases. Each participating center will decide internally which local investigator will be the principal investigator (PI) and who will be listed as a co-author/s within the writing committee should the center fulfil the criteria mentioned. The study coordinator (GW Kim) will be the first author. The corresponding authorship position is reserved for the project leader (JBYS). The last author position is reserved for the project co-leader (YWP). The remaining co-authors within this study group will be listed according to the number of patients recruited per center. The center with the highest recruitment numbers will take the second and third authorship positions. Any publication, presentation or abstract on collected data will be delegated to all authors. Each center keeps ownership of their own data and additional reports on data collected will only be conducted with written permission from each center's PI. All participating authors can suggest alterations to the study design or additional analyses. All the principal investigators together with the study coordinators and project leader constitute the steering committee of the project. These rules are subject to the verification that data collected from the recruited patients are complete and to the satisfaction of the study project leader and co-leader, with ranking priority given to centers with complete datasets.

10.2. Study group authorship

This group of co-authors will be collectively listed under the study group name (AI Multidisciplinary Tumour Study Group – AIM Study Group). This list of co-authors will be submitted, indexed and linked to any publication associated with this study group where possible. Centers who recruit at least 25 patients for this study will be eligible to include 2 co-authorship positions in this list. This will be in addition to the authorship positions given for centers that recruit at least 50 or 100 patients.

10.3. Acknowledgments

All centers that participate in this study are eligible to provide 2 names for acknowledgement in this study. This is in addition to the authorship positions given in the writing committee and study group for eligible centers.

11. REFERENCES

[1] Basta YL, Bolle S, Fockens P, Tytgat KMAJ. The Value of Multidisciplinary Team Meetings for Patients with Gastrointestinal Malignancies: A Systematic Review. Ann Surg Oncol. 2017 Sep;24(9):2669-2678. doi: 10.1245/s10434-017-5833-3.

[2] Specchia ML, Frisicale EM, Carini E et al. The impact of tumor board on cancer care: evidence from an umbrella review. BMC Health Serv Res 20, 73 (2020). doi: 10.1186/s12913-020-4930-3.

[3] Osheroff J, Teich J, Levick D. et al. Improving Outcomes with Clinical Decision Support: An Implementer's Guide. (HIMSS Publishing, 2012).

[4] An overview of clinical decision support systems: benefits, risks, and strategies for success

Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. NPJ Digit Med. 2020; 3: 17. Published online 2020 Feb 6. doi: 10.1038/s41746-020-0221-y.

[5] Kwok R, Dinh M, Dinh D, Chu M. Improving adherence to asthma clinical guidelines and discharge documentation from emergency departments: Implementation of a dynamic and integrated electronic decision support system. Emerg. Med. Australas. 2009;21:31–37.

[6] Somashekhar SP, Sepúlveda MJ, Puglielli S et al. Watson for Oncology and breast cancer treatment recommendations: agreement with an expert multidisciplinary tumor board. Ann Oncol. 2018 Feb 1;29(2):418-423. doi: 10.1093/annonc/mdx781.

[7] Zhou N, Zhang CT, Lv HY et al. Concordance Study Between IBM Watson for Oncology and Clinical Practice for Patients with Cancer in China. Oncologist. 2019 Jun;24(6):812-819. doi: 10.1634/theoncologist.2018-0255.

[8] Tian Y, Liu X, Wang Z et al. Concordance Between Watson for Oncology and a Multidisciplinary Clinical Decision-Making Team for Gastric Cancer and the Prognostic Implications: Retrospective Study. J Med Internet Res. 2020 Feb 20;22(2):e14122. doi: 10.2196/14122.

[9] Yao S, Wang R, Qian K, Zhang Y. Real world study for the concordance between IBM Watson for Oncology and clinical practice in advanced non-small cell lung cancer patients at a lung cancer center in China. Thorac Cancer. 2020 May;11(5):1265-1270. doi: 10.1111/1759-7714.13391.

[10] You HS, Gao CX, Wang HB et al. Concordance of Treatment Recommendations for Metastatic Non-Small-Cell Lung Cancer Between Watson for Oncology System and Medical Team. Cancer Manag Res. 2020 Mar 16;12:1947-1958. doi: 10.2147/CMAR.S244932.

[11] Zou FW, Tang YF, Liu CY, Ma JA, Hu CH. Concordance Study Between IBM Watson for Oncology and Real Clinical Practice for Cervical Cancer Patients in China: A Retrospective Analysis. Front Genet. 2020 Mar 24;11:200. doi: 10.3389/fgene.2020.00200.

12. List of Attachments

Appendix 1: Example of AIM Platform

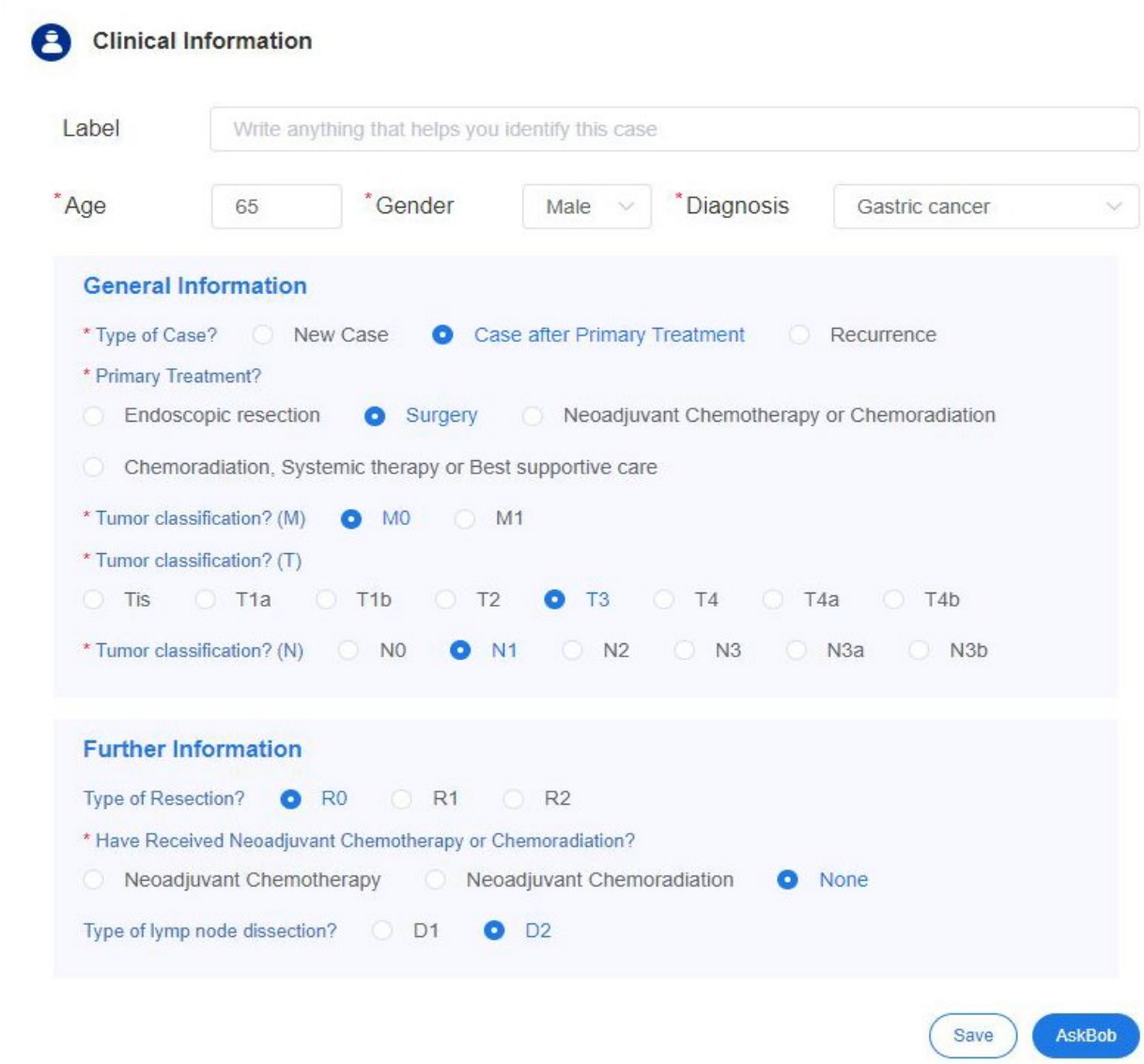


Figure 1. AIM Online Platform for Gastric Carcinoma

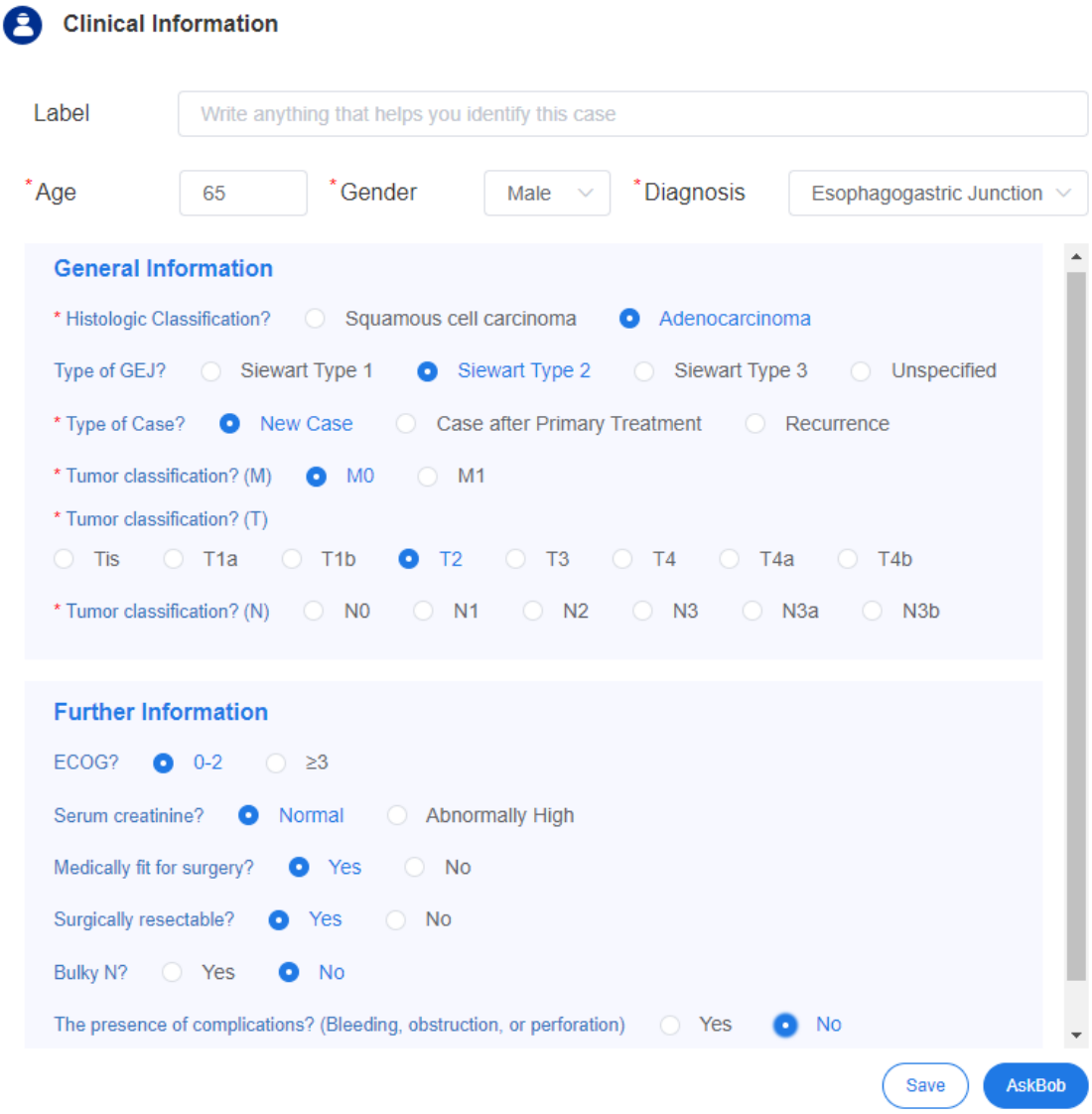


Figure 2. AIM Online Platform for GEJ Carcinoma

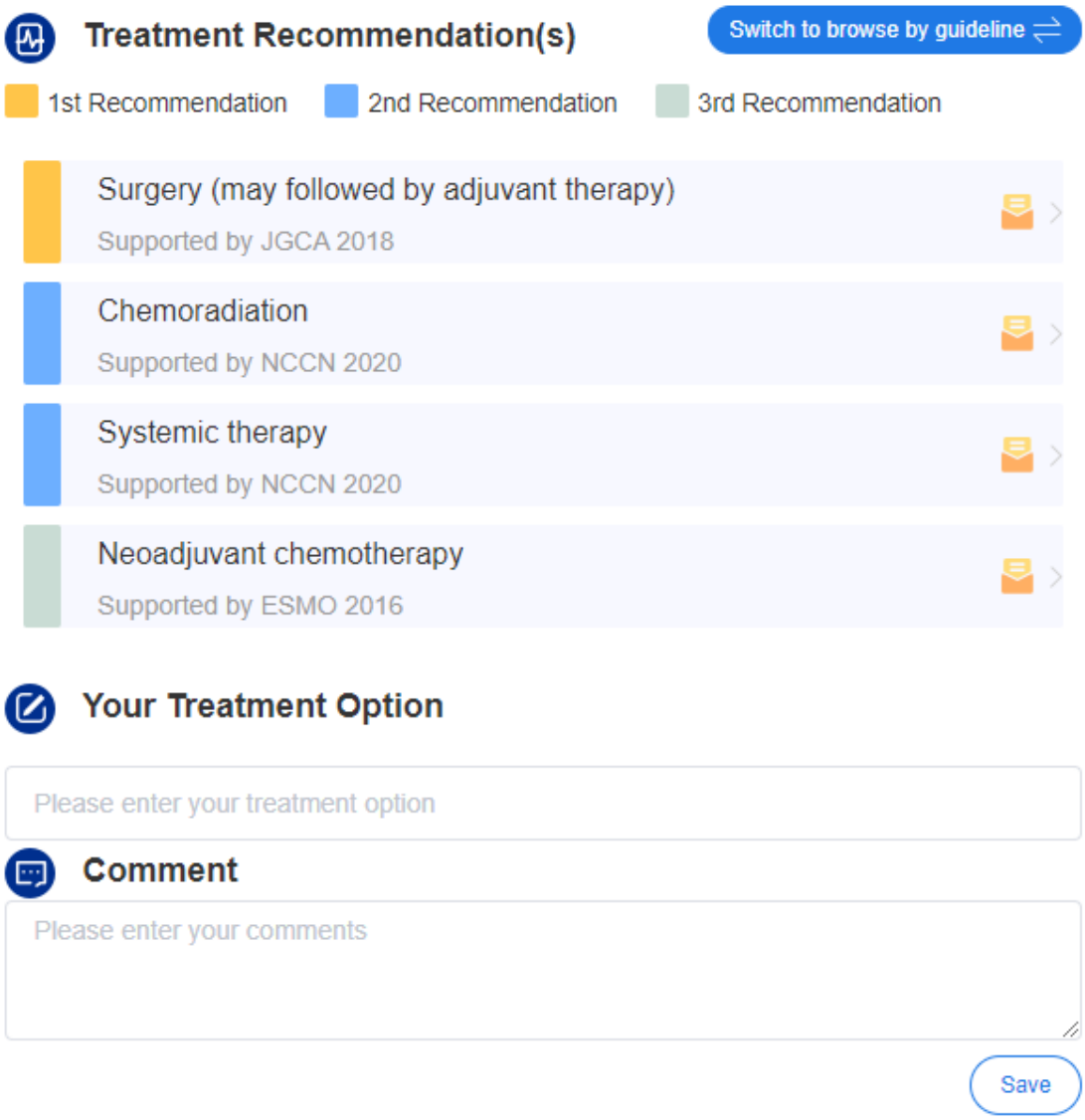


Figure 3. Example of AIM Treatment Recommendations

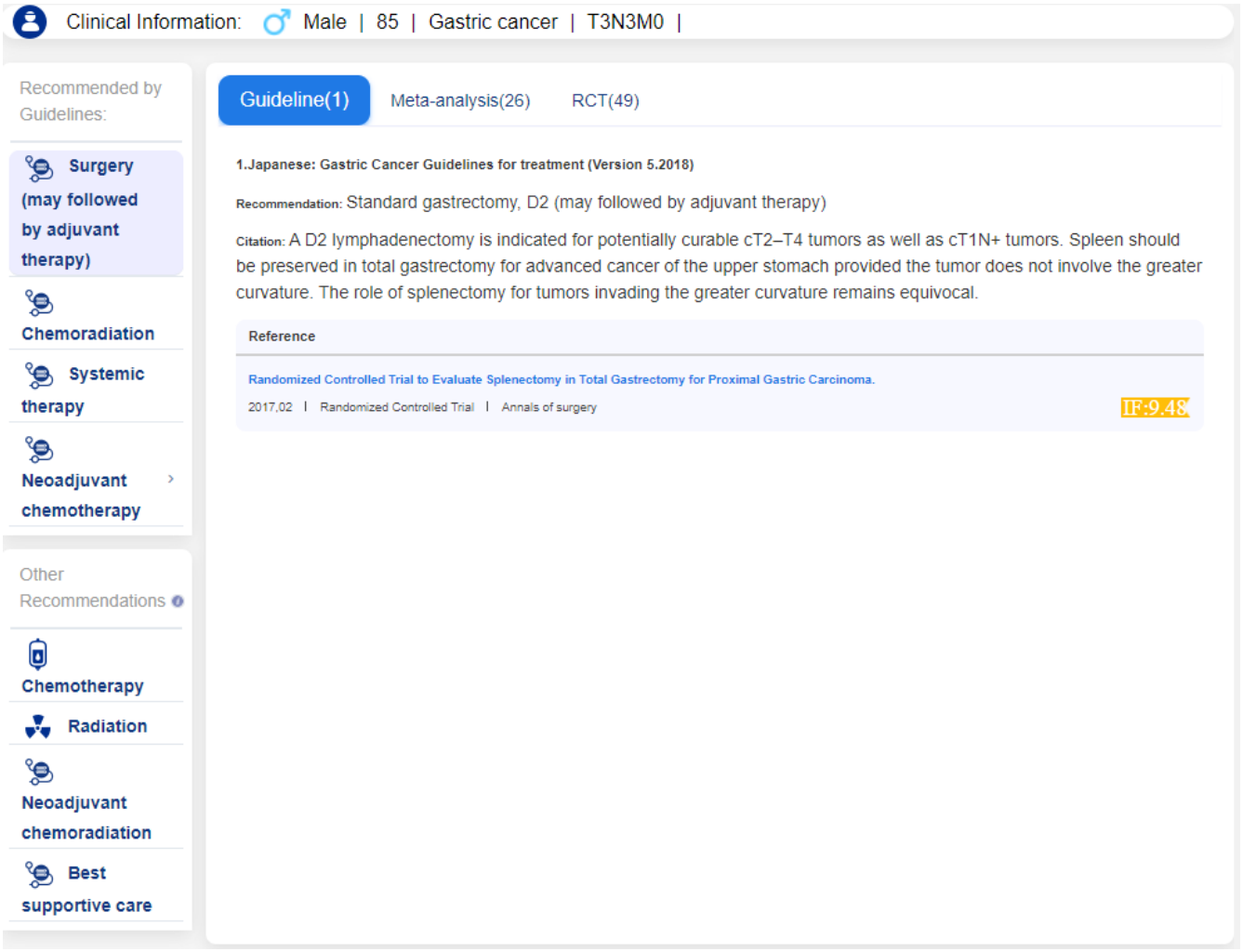


Figure 4. Example of AIM Reference Page

Appendix 2: Sample Patient Information Sheet and Informed Consent Form

INFORMED CONSENT FORM

1. Study Information

Protocol Title:
Development of a Clinical Decision Support System with Artificial Intelligence for Cancer Care

Principal Investigator & Contact Details:

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Associate Consultant
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Tel: (65) 6716 2000

Dr Aung Myint Oo
Consultant
Department of General Surgery
Tan Tock Seng Hospital (TTSH)
11 Jln Tan Tock Seng,
Singapore 308433

Tel: (65) 6256 6011

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Nevertheless, before you take part in this research study, the study will be explained to you and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign this informed consent form. You will be given a copy of this consent form to take home with you.

You are invited because your treatment plan is being discussed during the multidisciplinary molecular tumor board.

This study is carried out to validate a clinical decision support system with artificial intelligence for cancer care. This system is used to provide treatment recommendation for each upper gastric cancer or esophageal cancer patient based on their disease conditions.

This study will recruit 1000 subjects from different countries over a period of 3 years. About 150 subjects from NUH, 50 subjects from NTFGH and 100 subjects from TTSH will be involved in this study.

3. What procedures will be followed in this study

If you take part in this study, you will allow the study team members to collect your medical history, demographics, pathological data and your treatment plan.

Your participation in the study will last 3 years. You will not need to visit the doctor's office in the course of the study and all your clinic visits will be scheduled according to your clinical condition as per treatment guidelines.

Any individually-identifiable data obtained during the course of this study will be stored and

analysed for the purposes of this study and will not be used for future biomedical research. If you agree, your data may be shared with other collaborating researchers and/or institutions in a de-identified manner.

Your data collected during the study are coded and do not contain any identifying information that may link to you directly. All individually-identifiable information will be kept in a password-protected database which only the Principal Investigator and authorized personnel have access to.

“Incidental findings” are findings that have potential health or reproductive importance to research participants like you/your child and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study. There will not be any incidental findings arising in this research.

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by your primary physician. No additional visits or procedures are required in the participation of this study.

5. What Is Not Standard Care or is Experimental in This Study

The collection of clinical information during your visits are only being performed for the research and not part of your routine care. There is no experiment drug or procedure to be involved in this study.

The study is being conducted because the clinical decision support system with artificial intelligence for cancer care is developed but yet to be validated. We hope that your participation will help us to validate and improve this system in order to provide this service in multicenter with or without multi-disciplinary expertise.

6. Possible Risks and Side Effects

The anticipated risks and side effects of your participation in this study is minimal. Data collected will be de-identified using a unique code number and only study team member will have access to the patient identification. As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

7. Possible Benefits from Participating in the Study

There is no known benefit from participation in this study. However, your participation in this study may add to the medical knowledge about the use of this clinical decision support system with artificial intelligence for cancer care.

8. Alternatives to Participation

If you choose not to take part in this study, you will receive standard care for your condition. Your procedures will be performed as planned without the additional data collection.

9. Costs & Payments if Participating in the Study

If you take part in this study, the following will be performed at no charge to you: Data collection will be covered by the study. These costs of all procedures, as prescribed by your doctor because of your medical condition, as well as medicines and clinic consultations following this study will be on your personal expense. There will be no additional cost incurred by participating in this research and there will also be no reimbursement provided to you.

10. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, the data that have been collected until the time of your withdrawal will be kept and analyzed. The reason is to enable a complete and comprehensive evaluation of the study.

Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you *(or your legally acceptable representative, if relevant*) will be informed in a timely manner by the Principal Investigator or his/her representative.

11. Compensation for Injury

If you follow the directions of the doctors in charge of this study and you are physically injured due to the trial substance or procedure given under the plan for this study, the NUH/ NTFGH/ TTSH will pay the medical expenses for the treatment of that injury.

Payment for management of the normally expected consequences of your treatment will not be provided by the NUH/ NTFGH/ TTSH.

NUH/ NTFGH/ TTSH without legal commitment will compensate you for the injuries arising from your participation in the study without you having to prove NUH/ NTFGH/ TTSH is at fault. There are however conditions and limitations to the extent of compensation provided. You may wish to discuss this with your Principal Investigator.

By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

12. Confidentiality of Study and Medical Records

Your participation in this study will involve the collection of “Personal Data”. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. This includes

medical conditions, medications, investigations and treatment history.

Information and "Personal Data" collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available.

However, the study staff, NHG Domain Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you (*or your legally acceptable representative, if relevant*) are authorising (i) the collection, access to, use and storage of your "Personal Data", and (ii) the disclosure to authorised service providers and relevant third parties.

Data collected and entered into the Case Report Forms are the property of NUH/ NTFGH/ TTSH. In the event of any publication regarding this study, your identity will remain confidential.

Research arising in the future, based on your "Personal Data", will be subject to review by the relevant institutional review board.

Any information containing your "Personal Data" that is collected for the purposes described in this Informed Consent Form will not be stored in Singapore. Only anonymised data will be transferred out Singapore to Ping An Technology in the China.

By participating in this research study, you are confirming that you have read, understood and consent to the Personal Data Protection Notification available at http://www.nuhs.edu.sg/personal-data-protection/nuhsnuh-data-protection-policy.html, https://www.ttsh.com.sg/patient-guide/page.aspx?id=4468 and https://www.ntfgh.com.sg/JurongHealth/Personal_Data_Protection_Act.aspx.

13. Who To Contact if You Have Questions

If you have questions about this research study or any injuries during the course of this study, you may contact the Principal Investigators:

Prof Jimmy So Senior Consultant Department of Surgery, National University Hospital (NUH) 5 Lower Kent Ridge Road Singapore 119074 Tel: (65) 6779 5555	Dr Teh Jun Liang Associate Consultant Department of General Surgery Ng Teng Fong General Hospital (NTFGH) 1 Jurong East Street 21, Singapore 609606 Tel: (65) 6716 2000	Dr Aung Myint Oo Consultant Department of General Surgery Tan Tock Seng Hospital (TTSH) 11 Jln Tan Tock Seng, Singapore 308433 Tel: (65) 6256 6011

The study has been reviewed by the NHG Domain Specific Review Board (the central ethics committee) for ethics approval.

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain Specific Review Board Secretariat at 6471-3266. You can also find more information about participating in clinical research, the NHG Domain Specific Review Board and its review

processes at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

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CONSENT FORM

Protocol Title:
Development of a Clinical Decision Support System with Artificial Intelligence for Cancer Care

Principal Investigator & Contact Details:

Prof Jimmy So
Senior Consultant
Department of Surgery,
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Tel: (65) 6716 2000

Dr Aung Myint Oo
Consultant
Department of General Surgery
Tan Tock Seng Hospital (TTSH)
11 Jln Tan Tock Seng,
Singapore 308433

Tel: (65) 6256 6011

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction. I have also been informed and understood the alternative treatments or procedures available and their possible benefits and risks.

By participating in this research study, I confirm that I have read, understood and consent to the NUH/ NTFGH/ TTSH Personal Data Protection Notification.

_____	_____	_____
Name of Participant	Signature	Date

Witness Statement
I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant/ the participant's legally acceptable representative signing this informed consent form has the study fully explained in a language understood by him/ her and clearly understands the nature, risks and benefits of his/ her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant/ the participant's legally acceptable representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date

1. In accordance with Section 6(d) of the Human Biomedical Research Act and Regulation 25 of the Human Biomedical Research Regulations 2017, appropriate consent must be obtained in the presence of a prescribed witness who is 21 years of age or older, and has mental capacity. The witness must be present during the entire informed consent discussion, and must not be the same person taking the appropriate consent. The witness may be a member of the team carrying out the research.
2. However, if the participant/ the participant's legally acceptable representative is unable to read, and/ or sign and date on the consent form, an impartial witness should be present instead. The impartial witness should not be a member of the study team.

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

Name of Investigator / Person administering consent	Signature	Date

Appendix 3: ICMJE Criteria For Joined Authorship

Source: http://www.icmje.org/ethical_1author.html

The ICJME has recommended the following criteria for authorship; these criteria are still appropriate for journals that distinguish authors from other contributors.

- Authorship credit should be based on 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

- When a large, multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript (3). These individuals should fully meet the criteria for authorship/contributorship defined above, and editors will ask these individuals to complete journal-specific author and conflict- of-interest disclosure forms. When submitting a manuscript authored by a group, the corresponding author should clearly indicate the preferred citation and identify all individual authors as well as the group name. Journals generally list other members of the group in the Acknowledgments. The NLM indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript; it also lists the names of collaborators if they are listed in Acknowledgments.

- Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.

- All persons designated as authors should qualify for authorship, and all those who qualify should be listed. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content