Evaluation of EverLift in the Performance of Polypectomy for Polyps 4-9mm

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1. PURPOSE OF THE STUDY

a. Brief Summary

It is important to optimize complete resection of polyps as residual tissue may play a role in interval cancers. The US Multi-Society Task Force recommends diminutive (≤5 mm) and small (6–9 mm) polyps be removed by cold snare polypectomy (CSP). Use of viscous submucosal agents has not been evaluated in CSP. In this trial, we investigate the potential role of EverLift™ (GI Supply, Pennsylvania) in CSP.

b. Objectives

This study is a single-center, prospective noninferiority randomized clinical trial evaluating CSP for nonpedunculated polyps 4-9mm, with or without submucosal injection of EverLift™. The primary outcome is complete resection rate, defined by absence of residual polyp in the margin biopsies.

c. Rationale for Research in Humans

There are no effective animal endoscopy models that would allow real-time assessment of efficacy of polypectomy.

2. STUDY PROCEDURES

a. Procedures

If a polyp 4-9mm is to be removed as part of routine clinical care during the endoscopy procedure, we will remove half of the polyps using cold snare with submucosal injection of EverLift™ and the other half without submucosal injection of EverLift™. Biopsies will be performed at the margins of the polypectomy site. This will allow us to assess whether cold biopsy forceps or cold snare is more effective at adequately removing polyps. While biopsies are routinely performed in clinical practice to check for completeness of resection, the biopsies performed at the margins of the polypectomy site are done for research purposes. However, biopsies of the margins are of minimal increased risk.

b. Procedure Risks

The participants will have their regularly scheduled endoscopy procedures. Polyps will be removed as part of routine clinical practice. While biopsies are routinely performed in clinical practice to check for completeness of resection, the biopsies performed at the margins of the polypectomy site are done for research purposes. However, biopsies of the margins are of minimal increased risk.

c. Use of Deception in the Study

There is no deception in the study.

d. Use of Audio and Video Recordings

Endoscopy videos will be obtained. There will be no patient-identifying information on these videos. The videos may be shown at scientific meetings and will be kept as part of the study data.

e. Alternative Procedures or Courses of Treatment

The alternative is not to participate. In this case only the standard medically indicated endoscopic procedure will be performed.

f. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Yes. All patients will continue to receive their appropriate medical therapy.

g. Study Endpoint(s)

The primary outcome measured was completeness of resection, defined as absence of polyp tissue in both polypectomy site margin biopsies. This outcome was tested for noninferiority. Secondary outcomes included polypectomy time, number of snare attempts for polyp removal, use of hemostatic clips, complication rates.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

There is limited data looking at use of submucosal injection in polyps <10mm. In work by Zhang et al in 2018 evaluating CSP of polyps 6-9mm with or without submucosal injection of normal saline/epinephrine/indigo carmine, incomplete resection rate was significantly lower in the group with submucosal injection. However, in 2020 Shimodate compared CSP with or without submucosal injection of normal saline/indigo carmine/epinephrine for polyps 3-10mm. In this study, there was no difference in rates of complete muscularis mucosal resection. To date, there has been no study evaluating viscous submucosal lifting agents.[7]

Findings from Past Animal Experiments
There are no prior relevant animal experiments.

Radioisotopes or Radiation Machines

b. Standard of Care (SOC) Procedures

Identify Week/Month of Study	Name of Exam	Identify if SOC or Research
N/A	N/A	N/A

c. Radioisotopes

i. Radionuclide(s) and chemical form(s)

N/A

ii. Total number of times the radioisotope and activity will be administered (mCi) and the route of administration for a typical study participant

N/A

iii. If not FDA approved: dosimetry information and source documents (package insert, Medical Internal Radiation Dose [MIRD] calculation, and peer reviewed literature)

N/A

d. Radiation Machines – Diagnostic Procedures

i. Examination description (well-established procedures)

N/A

ii. Total number of times each procedure will be performed (typical study participant)

N/A

iii. Setup and techniques to support dose modeling

N/A

iv. FDA status of the machine and information on dose modeling (if procedure is not well-established)

N/A

e. Radiation Machines – Therapeutic Procedures

i. Area treated, dose per fraction/number of fractions, performed as part of normal clinical management or due to research participation (well-established procedures)

N/A

ii. FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions (if procedure is not well-established)

N/A

4. DEVICES USED IN THE STUDY

a. Investigational Devices (Including Commercial Devices Used Off-Label)

N/A

b. IDE-Exempt Devices

N/A

5. DRUGS, BIOLOGICS, REAGENTS, OR CHEMICALS USED IN THE STUDY

a. Investigational Drugs, Biologics, Reagents, or Chemicals

N/A

b. Commercial Drugs, Biologics, Reagents, or Chemicals

N/A

6. DISINFECTION PROCEDURES FOR MEDICAL EQUIPMENT USED ON BOTH HUMANS AND ANIMALS

N/A

7. PARTICIPANT POPULATION

a. Planned Enrollment

Papastergiou et al found that cold snare endoscopic mucosal resection of polyps 6-10mm had complete resection 92.8% of polypectomies. Using this data, in our sample size calculation we determined 115 polyps would be needed in each group to achieve an alpha value of 0.05, power of 90%, and non-inferiority margin of -10%.

b. Age, Gender, and Ethnic Background

Age $\geq$ 18, including all genders and ethnic backgrounds.

c. Vulnerable Populations

No vulnerable subjects.

d. Rationale for Exclusion of Certain Populations

Children are not included because the endoscopy units only serve adult patients

e. Stanford Populations

N/A

f. Healthy Volunteers

N/A

g. Recruitment Details

Patients who are scheduled for endoscopy by one of the investigators will be asked if they are interested in participating in the study.

h. Eligibility Criteria

i. Inclusion Criteria

Patients 18 years or older undergoing colonoscopy, who had 1 or more polyps of the correct size 4-9mm that were removed.

ii. Exclusion Criteria

Patients <18 or >80; patients with inflammatory bowel disease or polyposis syndromes; patients who did not have consent form; patients in whom polyps were not removed.

i. Screening Procedures

Patients scheduled for endoscopy by one of the investigators will be asked if they would like to participate in the study. If they are interested, then they will be enrolled.

j. Participation in Multiple Protocols

We will ask all patients if they are participating in any other studies. If they are participating in any other studies then we will ask them for more information to determine whether there could be any harm from participating in both studies and if there is then they will not be enrolled.

k. Payments to Participants

No payment.

l. Costs to Participants

No costs.

m. Planned Duration of the Study

1 year.

8. RISKS

a. Potential Risks

i. Investigational devices

N/A

ii. Investigational drugs

N/A

iii. Commercially available drugs, biologics, reagents or chemicals

N/A

iv. Procedures

There is a very low (< 1 in 5000) risk of perforation of the gastrointestinal tract and a low (< 1 in 1000) risk of bleeding during the study portion of the endoscopy. There is a very low risk of an adverse event from the blood draw (< 1 in 1000). There is a very low risk of an adverse event from biopsies of resection site (<1 in 1000 risk of bleeding, <1 in 1000 risk of infection). There is a very low risk of adverse event from polypectomy of a small polyp - there is no evidence to suggest either technique (cold snare or cold biopsy) is safer than the other.

v. Radioisotopes/radiation-producing machines

N/A

vi. Physical well-being

With the exception of the rare potential complications described above, we do not expect any harm to the participants' physical well-being.

vii. Psychological well-being

The patients are sedated during their medically-necessary endoscopy procedures and we do not expect any harm to their psychological health.

viii. Economic well-being

No expected effect

ix. Social well-being

No expected effect

x. Overall evaluation of risk

Low

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b. International Research Risk Procedures

N/A

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c. Procedures to Minimize Risk

All of the patients undergo continuous vital signs monitoring by trained endoscopy nurses during the procedure. They are monitored continuously during the procedure and during recovery for any evidence of complications.

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d. Study Conclusion

The study will be completed during the endoscopy procedure.

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e. Data Safety Monitoring Plan (DSMC)

i. Data and/or events subject to review

Complications from the endoscopy, including any complications that could potentially be due to the study.

ii. Person(s) responsible for Data and Safety Monitoring

The investigators and protocol director will be responsible for monitoring the data

iii. Frequency of DSMB meetings

Possible adverse events will be reviewed daily.

iv. Specific triggers or stopping rules

If any adverse events occur, the protocol will be suspended until the PD investigates the event and determines whether or not it is related to the study.

v. DSMB Reporting

The PD will inform the IRB if any adverse events relating to the study occur.

vi. Will the Protocol Director be the only monitoring entity? (Y/N)

The Protocol Director will be the only monitoring entity for this study.

vii. Will a board, committee, or safety monitor be responsible for study monitoring? (Y/N)

No

f. Risks to Special Populations

N/A

9. BENEFITS

This study will potentially improve our ability to treat premalignant disorders of the GI tract.

10. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.