



Non-hepatic Cancer and Liver Transplantation: Shifting the Paradigm. Dropping the Cancer Stigma.

INTRODUCTION

A significant and growing number of patients in need of liver transplantation (LT) have a history of cancer. Management of these patients is challenging, as history of a pre-transplant malignancy (PTM) in remission has long been considered a relative contraindication due to the concern that immunosuppression required to prevent graft rejection would allow the growth of dormant malignant cells in these patients. Recommendations for listing transplant candidates with PTM were based primarily on the recurrence rates in kidney transplant recipients derived from the Israel Penn International Transplant Tumour Registry (IPITTR, previously known as the Cincinnati Transplant Tumour Registry), a voluntary database of transplant recipients with malignancies. Data from the IPITTR indicated that the recurrence rate of PTM was 21% or a rate of 5.6 cancer recurrences per 100 person/year of follow-up, and that most recurrences (53%) occurred in those transplanted within two years of a cancer diagnosis or treatment. However, these studies were done decades ago, and several more recent population-based cohort studies and systemic reviews with meta-analyses have reported markedly lower rates of recurrence in recipients with PTM.

Currently, guidelines for the selection of liver transplant candidates generally recommend minimum wait-times before

transplantation for patients with PTM that range from no waittime for some in situ malignancies to more than five years for melanoma, bladder, colorectal, and breast cancer, provided that the neoplasms have been eradicated and that the oncologic expected survival is superior to the survival expected after LT. Unfortunately, most of the guidelines are based on data from the kidney transplantation arena and do not take substantial recent improvements in cancer therapy (including immunotherapy) into consideration.

In addition, as older donors are increasingly utilized, the risk of non-liver cancer in some of these donors, either in the past medical history or found incidentally after donation has also increased, and it must be established how to manage recipients transplanted with these organs.

Finally, de novo cancer is one of the most frequent causes of death in liver transplant recipients with studies showing an association between cumulated immunosuppression and risk of cancer.

In essence, the increasing number of liver transplant candidates with a history of cancer, and that of recipients who develop cancer post-transplantation, together with the improvement in oncology therapy, calls for a more thorough evaluation of the risk of post-transplant cancer development as well as management of these patients.

ILTS President

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Claus Niemann, MD UCSF, San Francisco, USA **ILTS President-Elect** 2020-21

Marina Berenguer, MD La Fe University

Spain

Hospital, Valencia,

ILTS President-Elect 2021-22

Mohamed Rela, MS FRCS, DSc Dr. Rela Institute and Medical Center, Chennai India

ILTS-SETH 2021 Consensus Conference Topic Coordinators:

Kymberly Watt, MD Mayo Clinic, Rochester, USA

Mark

Jordi Colmenero, MD, PhD Hospital Clinic Barcelona. Barcelona, Spain

SETH President

José Antonio Pons, MD, PhD

Virgen de la Arrixaca University Hospital, Murcia, Spain





Non-hepatic Cancer and Liver Transplantation: Shifting the Paradigm. Dropping the Cancer Stigma.

In this Consensus Conference, we will discuss:

- How to evaluate the presence of malignancies in liver transplant candidates;
- The risk and post-LT surveillance for those with a history of pre-transplant malignancy in remission;
- Who is safe to donate a liver with a history of cancer (deceased or live donor/cancer detected during donor work-up) and what could be done if the recipient develops a malignancy transmitted from a donor;
- Factors that increase the risk of post-transplant non-hepatic malignancies and how to manage immunosuppression and onco-specific therapies in these patients;
- Whether surveillance is cost-beneficial in high-risk individuals:
- · Whether the data applies to pediatrics.

LEARNING OBJECTIVES

- 1. Understand the gap between current practice and future transplant-related oncology.
- Update selection criteria and prediction models in candidates with a history of prior malignancy in remission.
- Identify when it is safe to donate a liver from a candidate with a history of cancer or with cancer detected during the transplant work-up.
- Identify novel biological, chemotherapeutic, radiological, and immunotherapeutic approaches for patients with de novo cancer developing after liver transplantation.

EXPECTED EDUCATIONAL OUTCOMES

The participants will be able to review and discuss research regarding non-hepatic malignancy in the candidate, the donor or the recipient, including selection criteria/indications, prognostic models, surveillance strategies, novel therapies and management. The participants will gain insight into innovations that lead to improvement in the field of liver transplantation in candidates or donors with a history of malignancy, and in recipients with de novo cancer, both in adult and pediatric populations.

TARGET AUDIENCE

- Surgeons
- Hepatologists
- Pathologists
- Radiologists
- Oncologists
- Scientists
- Nurses





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Scientific Program | Thursday, January 28, 2021

13:00 - 18:10	Consensus Conference Lectures (Open to all participants)
13:00 - 13:10	Introduction José Antonio Pons, MD, PhD Virgen de la Arrixaca University Hospital, Murcia, Spain
13:10 - 14:40	General Concepts Chairs: Marina Berenguer, MD La Fe University Hospital, Valencia, Spain José Antonio Pons, MD, PhD Virgen de la Arrixaca University Hospital, Murcia, Spain
13:10 - 13:25	Liver transplantation outcomes and current candidates profile Nazia Selzner, MD, PhD University of Toronto, Toronto, Canada
13:25 - 13:40	Outlining the current approach to non-hepatic cancer in LT John Roberts, MD UCSF, San Francisco, USA
13:40 - 13:55	Role of immunosuppression in cancer Manuel Rodriguez-Perálvarez, MD, PhD Reina Sofia University Hospital, Cordoba, Spain
13:55 - 14:10	New anti-cancer therapies: Beyond the conventional multidisciplinary cancer care Milind Javle, MD University of Texas MD Anderson Cancer Center, Houston, USA
14:10 - 14:40	Q&A
14:40 - 14:55	Break
14:55 - 16:10	Pre-transplant Considerations: Work-up for Recipient and Donor Candidates Chairs: Itxarone Bilbao, MD Vall d'Hebron University Hospital, Barcelona, Spain Mohamed Rela, MS, FRCS, DSc Dr. Rela Institute and Medical Center, Chennai, India
14:55 - 15:10	How to manage LT candidates with a history of cancer/newly diagnosed cancer during pre-transplant work-up? Sergio A. Acuna, MD, PhD University of Toronto, Toronto, Canada
15:10 - 15:25	How to proceed with deceased donors with a history of cancer/cancer-like lesions found at the time of procurement? Beatriz Domínguez-Gil, MD, PhD National Transplant Organization, Madrid, Spain
15:25 - 15:40	How to proceed with living donors with a history of cancer or precancerous lesions/early-stage cancer found at the time of evaluation? Dong-Hwan Jung, MD, PhD Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
15:40 - 16:10	Q&A
16:10 - 16:25	Break





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16:25 - 17:55	Post-transplant Considerations: De Novo Malignancies in LT Recipients Chairs: Gonzalo Crespo, MD Hospital Clinic de Barcelona, Barcelona, Spain Mark Ghobrial, MD, PhD, FRCS Houston Methodist Hospital, Houston, USA
16:25 - 16:40	Incidence and risk factors Kymberly Watt, MD Mayo Clinic, Rochester, USA
16:40 - 16:55	Screening strategies after liver transplantation José Ignacio Herrero, MD University Clinic of Navarra, Pamplona, Spain
16:55 - 17:10	Treatment for solid tumors Gonzalo Sapisochin, MD UHN - Toronto General Hospital, Toronto, Canada
17:10 - 17:25	Treatment for post-transplant lymphoproliferative disorders (PTLD) Dok Hyun Yoon, MD Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
17:25 - 17:55	Q&A
17:55 - 18:10	Presidential address Claus Niemann, MD UCSF, San Francisco, USA





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Scientific Program | Friday, January 29, 2021

13:00 - 16:30 Afternoon Working Groups

(Working Group participation is limited to 30 pre-registered participants per group. Final selection will be made by the Topic Coordinators)

13:00 - 13:15 Introduction

Topic coordinators:

Jordi Colmenero, MD, PhD Hospital Clinic Barcelona, Barcelona, Spain Kymberly Watt, MD Mayo Clinic, Rochester, USA

Working Group 1: Non-hepatic Cancer in LT Candidates

Working Group Coordinators:

Magdalena Salcedo, MD, PhD Gregorio Marañón General University Hospital, Madrid, Spain Pål-Dag Line, MD, PhD Rikshospitalet, Oslo, Norway

Working Group Members:

Milind Javle, MD University of Texas MD Anderson Cancer Center, Houston, USA María Trapero, MD, PhD Autonomous University of Madrid, Madrid, Spain Francisco Javier Bustamante, MD Cruces University Hospital, Bilbao, Spain Carmen Vinaixa, MD La Fe University Hospital, Valencia, Spain Paolo de Simone, MD University of Pisa Medical School Hospital, Pisa, Italy

- 1.1. Evaluation of candidates. Timing to transplantation (tumor staging, treatments...)
- 1.2. Immunotherapy before the transplant: Specific measures at transplantation
- 1.3. Management after liver transplantation (immunosuppression, lifestyle and habits)
- 1.4. Specific considerations for each type of cancer

Working Group 2: De novo Malignancies after LT

Working Group Coordinators:

Jordi Colmenero, MD, PhD Hospital Clinic Barcelona, Barcelona, Spain Kymberly Watt, MD Mayo Clinic, Rochester, USA

Working Group Members:

Manuel Rodriguez-Perálvarez, MD, PhD Reina Sofia University Hospital, Cordoba, Spain José Ignacio Herrero, MD University Clinic of Navarra, Pamplona, Spain Sherrie Bhoori, MD National Cancer Institute of Milan, Milan, Italy Marco Senzolo, MD University Hospital of Padua, Padua, Italy

Prashant Bhangui, MBBS, MS Institute of Liver Transplantation and Regenerative Medicine, Medanta, Gurgaon, India

- 2.1. Epidemiology, risk factors and survival
- 2.2. Preventive strategies, surveillance of extrahepatic cancers
- 2.3. Management of immunosuppression in patients with de novo cancer





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Working Group 3: Prevention and Management of Donor-derived Malignancies after LT (Deceased and Living Donors)

Working Group Coordinators:

Beatriz Domínguez-Gil, MD, PhD National Transplant Organization, Madrid, Spain François Durand, MD, PhD University Paris VII, Paris, France

Working Group Members:

María Trinidad Serrano, MD, PhD Lozano Blesa University Hospital Clinic, Zaragoza, Spain José Manuel Asencio, MD, PhD, FACS Gregorio Marañón General University Hospital, Madrid, Spain Marieke Van Rosmalen, MD Eurotransplant International Foundation, Leiden, The Netherlands Julie Heimbach, MD Mayo Clinic, Rochester, USA

Taizo Hibi, MD, PhD, FACS Kumamoto University Graduate School of Medical Sciences, Kumamoto, Japan Olivier Detry, MD, PhD University of Liège, Liège, Belgium

Kerstin Mönch, MD Westpfalz-Hospital, Kaiserslautern, Germany

Christopher Watson, MD, PhD University of Cambridge, Cambridge, United Kingdom

- 3.1. Epidemiology and risk factors surveillance
- 3.2. How to minimize the occurrence of donor transmitted malignancies in liver transplant recipients
- 3.3. Specificities of the live liver donor with regards to donor transmitted malignancies
- 3.4. Assessment of risk and management based on individual tumor types
- 3.5. How to proceed in case of a suspected malignancy transmission (including early re-transplantation)

Working Group 4: Non-hepatic Cancer in the Pediatric Population

Working Group Coordinators:

Itxarone Bilbao, MD Vall d'Hebron University Hospital, Barcelona, Spain
Mohamed Rela, MS, FRCS, DSc. Dr. Rela Institute and Medical Center, Chennai, India

Working Group Members:

Francisco Hernández-Oliveros, MD, PhD University Hospital La Paz, Madrid, Spain Jesús Quintero, MD Vall d'Hebron University Hospital, Barcelona, Spain Paolo Muiesan, MD Elizabeth Hospital Birmingham, Birmingham, UK Mureo Kasahara, MD National Center for Child Health and Development, Tokyo, Japan

- 4.1. Extrahepatic solid tumors before pediatric LT
- 4.2. Leukemia, lymphoma and other hematologic disturbances before pediatric LT
- 4.3. Malignancies following pediatric LT, different approaches to post-transplant lymphoproliferative disorder

Working Group 5: Onco-specific Therapies after LT

Working Group Coordinators:

Mikel Gastaca, MD Cruces University Hospital, Bilbao, Spain Parissa Tabrizian, MD, MSc Icahn School of Medicine at Mount Sinai, New York, USA

Working Group Members:

Gonzalo Sapisochin, MD UHN - Toronto General Hospital, Toronto, Canada
Sonia Pascual, MD, HGU Alicante, Alicante, Spain
David James Pinato, MD, PhD Imperial College London, London, UK
David Al-Adra, MD, PhD University of Wisconsin School of Medicine and Public Health, Madison, USA
Henrik Petrowsky, MD, FACS University Hospital Zurich, Zurich, Switzerland
Laura A Dawson, MD, FRCPC, FASTRO Princess Margaret Cancer Centre/University Health Network,
University of Toronto, Toronto, Canada

- 5.1. Surgical management
- 5.2. Oncological medical therapy including immunotherapy post LT
- 5.3. Radiological therapies post LT





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Scientific Program | Saturday, January 30, 2021

13:00 - 16:00	Working Group Presentations (Open to all participants)
13:00 -14:30	Working Group Presentations with Summarizing Statements
13:00 - 13:30	Working Group 1 - Summarizing Statements and Q&A
13:30 - 14:00	Working Group 2 - Summarizing Statements and Q&A
14:00 - 14:30	Working Group 3 - Summarizing Statements and Q&A
14:30 - 14:45	Break
14:45 - 15:45	Working Group Presentations with Summarizing Statements
14:45 - 15:15	Working Group 4 - Summarizing Statements and Q&A
15:15 - 15:45	Working Group 5 - Summarizing Statements and Q&A
15:45 - 16:00	Consensus Conclusion





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The International Liver Transplantation Society (ILTS) and Spanish Liver Transplantation Society (SETH) jointly prepared this Consensus Conference:

Topic Coordinators:

- · Jordi Colmenero, MD, PhD Hospital Clinic Barcelona, Barcelona, Spain (SETH)
- Kymberly Watt, MD Mayo Clinic, Rochester, USA (ILTS)

Steering Committee Members:

- · José Antonio Pons, MD, PhD Virgen de la Arrixaca University Hospital, Murcia, Spain (SETH)
- · Magdalena Salcedo, MD, PhD Gregorio Marañón General University Hospital, Madrid, Spain (SETH)
- Itxarone Bilbao, MD Vall d'Hebron University Hospital, Barcelona, Spain (SETH)
- Mikel Gastaca, MD Cruces University Hospital, Bilbao, Spain (SETH)
- Prashant Bhangui, MBBS, MS Institute of Liver Transplantation and Regenerative Medicine, Medanta, Gurgaon, India (ILTS)
- Eleonora De Martin, MD Hospital Paul Brousse, Villejuif, France (ILTS)
- · Roberto Hernandez-Alejandro, MD, FACS, FRCSC University of Rochester Medical Center, Rochester, USA (ILTS)
- · Mina Komuta, MD Keio University, Tokyo, Japan (ILTS)

ILTS President 2019 - 2020:

· Claus Niemann, MD UCSF, San Francisco, USA

ILTS President-Elect 2020 - 2021:

· Marina Berenguer, MD La Fe University Hospital, Valencia, Spain

ILTS President-Elect 2021 - 2022:

· Mohamed Rela, MS, FRCS, DSc Dr. Rela Institute and Medical Center, Chennai, India





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CONTINUING MEDICAL EDUCATION (CME) CREDITS

The ILTS-SETH Consensus Conference on Non-hepatic Cancer and Liver Transplantation, Berlin (streamed live), Germany, 28/01/2021-30/01/2021 has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with 9 European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

Through an agreement between the Union Européenne des Médecins Spécialistes and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME® credit to AMA credit can be found at www.ama-assn.org/education/earn-credit-participation-international-activities.

Live educational activities, occurring outside of Canada, recognised by the UEMS-EACCME® for ECMEC®s are deemed to be Accredited Group Learning Activities (Section I) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.





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ILTS acknowledges the generous support of Natera



ILTS acknowledges the generous support of Novartis



This program has been supported by AstraZeneca through an unrestricted educational grant







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Consensus Conference Satellite Session by Natera

Topic

Advances in Molecular Residual Disease Assessment and Potential Applications in Liver Transplant Oncology

Introduction:

Identification of patients who achieved successful curative intent surgery continues to be a clinical challenge. Accurate identification of such patients could lead to treatment optimization with potential side-effect reduction, better resource allocation and improvement in quality of life and survival. Low levels of Circulating tumor DNA (ctDNA in the "sea" of normal DNA makes it challenging to detect molecular residual disease(MRD) in early-stage cancer. A tumor-informed approach where a sample of the patient's tumor tissue and a patient's blood sample is analyzed for germline mutations allows for increased sensitivity and specificity to find low levels of ctDNA in the background of cell free DNA. ctDNA has proven to be a clinically useful tool to determine residual molecular disease after surgery in early stage colorectal cancer and oligometastatic disease. Additionally treatment monitoring with reliable ctDNA marker can help stratify patients.

Objectives:

The objectives for this presentation will be to:

- 1. Provide an overview of Signatera's personalized ctDNA assay
- 2. Summarize clinical evidence in early stage and metastatic diseases, and
- 3. Discuss how this assay can change the paradigm of clinical care and clinical trial design in liver transplant oncology

Speaker:

Angel Rodriguez, MD Medical Oncology Director Natera

Date:

February 05, 2021

Time

17:30 -17:50 CET

How to join on February 5!

Join via Zoom:

https://us02web.zoom.us/j/83563894622?pwd=OHpEbDl6UWxMdkk5b1pScWMzSIFYZz09

Meeting ID: 835 6389 4622 Passcode: 485042

Join via Phone:

Find your local phone number: https://us02web.zoom.us/u/kdl5ozVIcB

Meeting ID: 835 6389 4622 Passcode: 485042

ILTS acknowledges the generous support of Natera







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TIME AND DATE

Consensus Conference Lectures

January 28, 2021 13:00 - 18:10

Working Groups

January 29, 2021 13:00 - 16:30

Working Group Presentations with Summarizing Statements / Consensus Conclusions

January 30, 2021 13:00 - 16:00

Time Zone

CET (Central European Time)
Check corresponding international time zones here.

ILTS HEADQUARTERS

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REGISTRATION

Please register here by January 28, 2021.

Should you require further assistance, please don't hesitate to contact the ILTS Registration Department:

E-mail: <u>registration-consensus@ilts.org</u> Hotline: +49 (0) 30 24603 410

www.ilts.org

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