DIFFERENTIAL BENEFITS OF DAAs IN DIFFERENT PATIENT POPULATIONS.
IN PATIENTS ON A WAITING LIST FOR TRANSPLANTATION. THE CLINIC.

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Disclosures

Honoraria for consulting or speaking (last 5 years):

AbbVie, BMS, Gilead, Janssen-Cilag, Medtronic, Merck/Schering-Plough, Norgine, Roche

Research grants (last 5 years):

BMS, Janssen Cilag, Medtronic, Roche

1. Why should we treat?
2. Who should we treat?
3. How should we treat?
4. No time to waste or wait to treat,
   i.e. after liver transplantation?

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1. Why should we treat?

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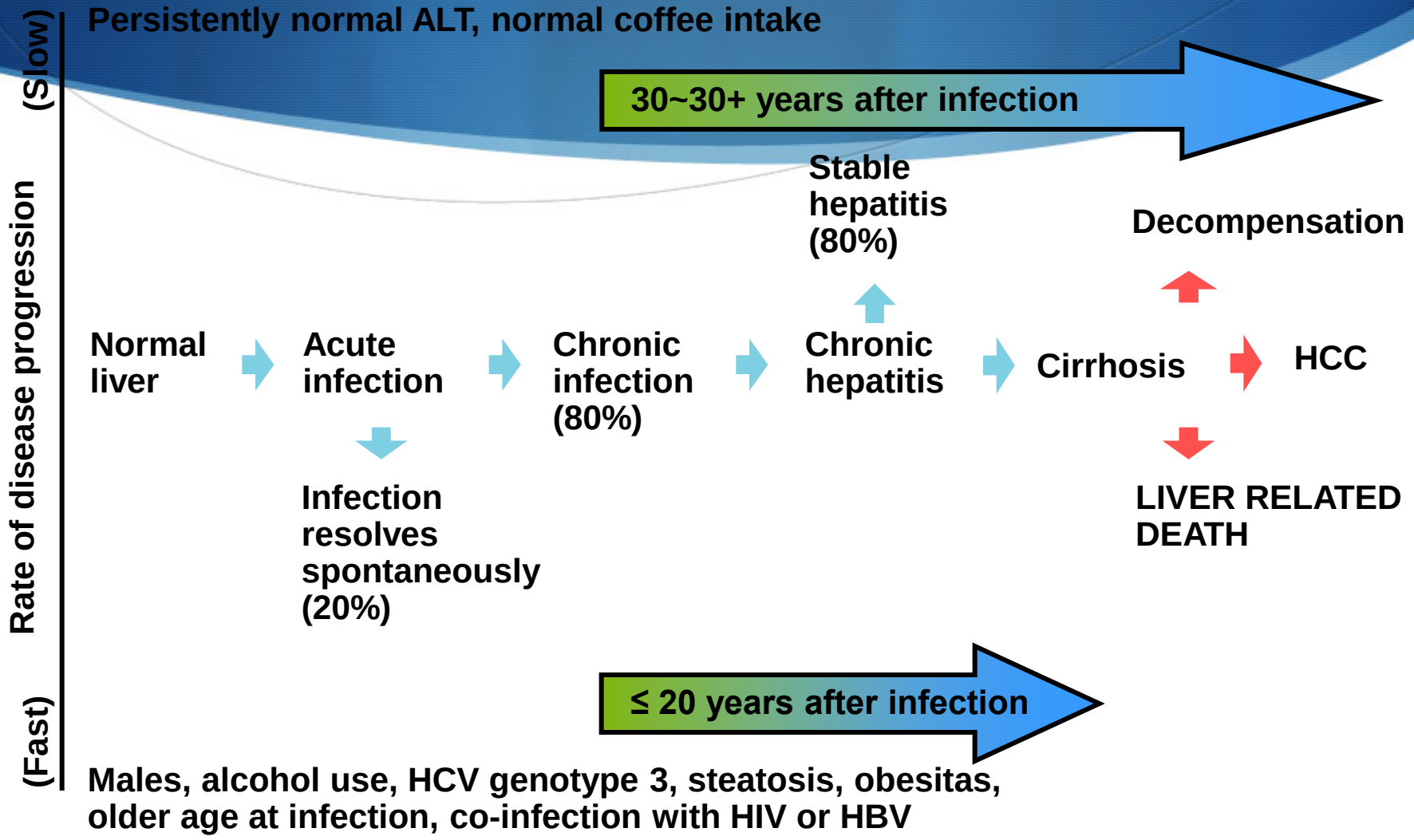
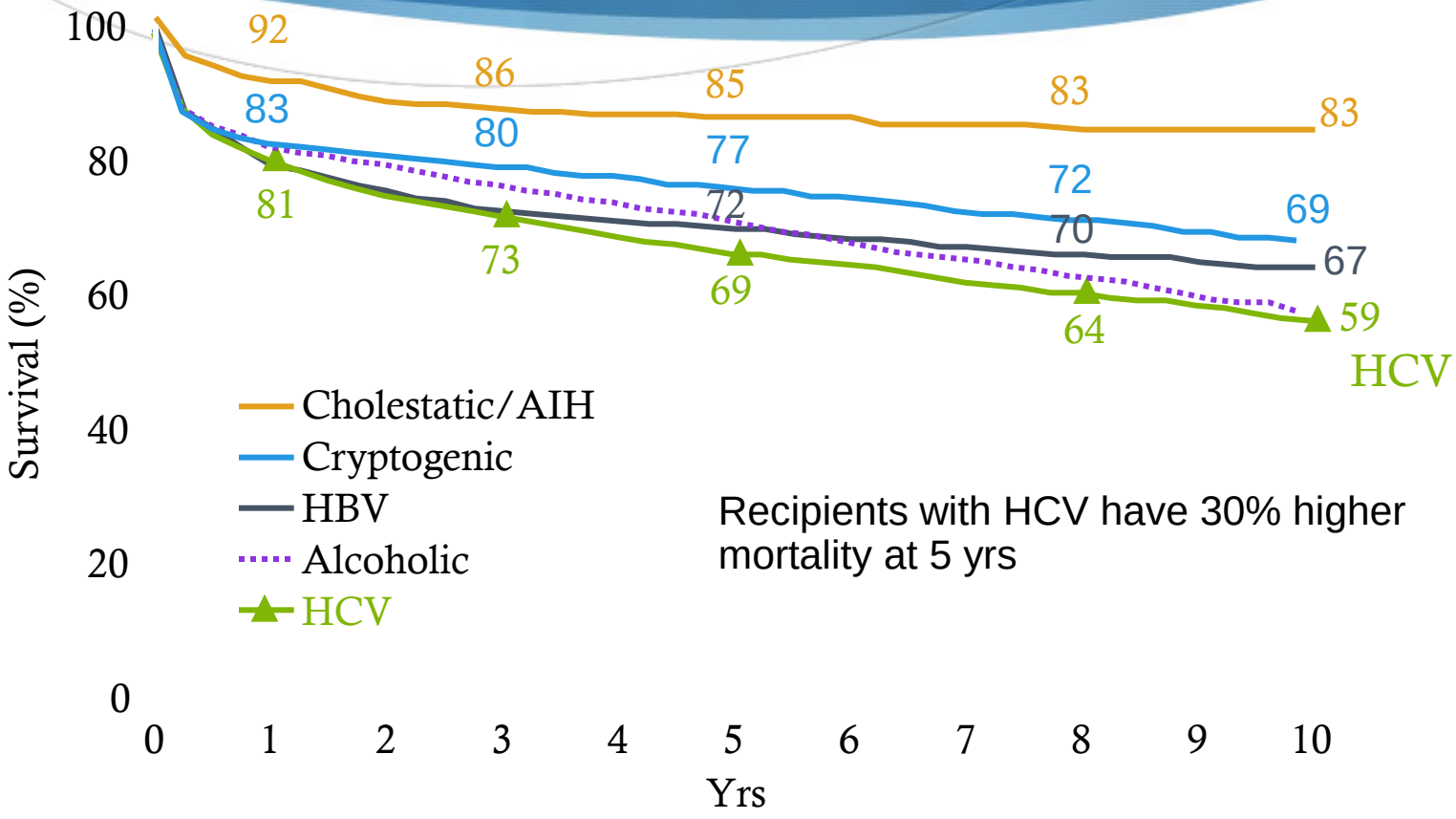
HCV is a slowly progressing disease



After liver transplantation HCV is a rapidly progressing disease



ELTR- 1/1988 - 12/2001

Forman LM, et al. Gastroenterology. 2002;122:889-896.

2. Who should we treat?

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Characteristics of patients on the waiting-list for liver transplantation

- Patients with compensated cirrhosis:
- - Child-Pugh A, low MELD-score
- - Hepatocellular carcinoma

- Patients with decompensated cirrhosis
- - Child-Pugh B-C, high MELD-score
- - ascites, portal hypertension, low nutritional status etc.

3. How should we treat?

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The goal of antiviral therapy

- SVR is not the goal of antiviral therapy

- We treat patients in order to:
  - Increase health-related quality of life
  - Reduce liver-related morbidity
  - Improve life expectancy

Patient and compound characteristics affecting choice of therapy

- Severity of liver disease (Child-Pugh A, B, vs. C)
- Previous treatment (peg/riba failure, PI-failure)
- HCV genotype
- SVR rates vs. body of evidence

DAAs in HCV liver cirrhosis
Current situation

Compounds	Genotype	CP-A	CP-B/C	Evidence
SOF/RIBA	GT2	78-91%/12w		Moderate
	GT3	62-92%/24w		Moderate
SOF/LDP/RIBA	GT1	96-100%/12w+RIBA	GT1 and GT4:86-90%, low	High
		97-100%/24w+RIBA		High
SOF/SIM/RIBA	GT1, Target	80-88%	<75%	High
	Cosmos	93-100%		Low
SOF/DAC/riba	GT3	58-61%		High
3D/riba	GT1	92%/12w		High
		97%/24w		High

DAAs in HCV liver cirrhosis

- Longer duration of therapy 24 weeks and/or addition of ribavirin:
- Peg/riba non-responders with IL28B TT
- GT1a vs. GT1b
- Previous null-responders to peg/riba

Clinical cases, patient 1

- 48-year old man, GT3
- Previous alcohol abuse
- HCC/RFA, recurrent HCC
- Relapse after peg/riba
- Treatment?

DAAs in HCV liver cirrhosis
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	Cosmos	93-100%		Low
SOF/DAC/riba	GT3	58-61%		High
3D/riba	GT1	92%/12w		High
		97%/24w		High

Clinical cases, patient 2

- 62-year old female, GT1b
- Controlled ascites/diuretics, 2x variceal bleeding
- Thrombocytes 70x10log9; albumin 36 g/L; bilirubin 58 mcmol/L; INR 1,2;creatin 82 mcmol/L. CPB8/MELD13.
- Breakthrough telaprevir/peg/riba
- Treatment?

DAAs in HCV liver cirrhosis
Current situation

Compounds	Genotype	CP-A	CP-B/C	Evidence
SOF/RIBA	GT2	78-91%/12w		Moderate
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	Cosmos	93-100%		Low
SOF/DAC/riba	GT3	58-61%		High
3D/riba	GT1	92%/12w		High
		97%/24w		High

Clinical cases, patient 3

- 62-year old female, GT1a
- HCC/RFA, recurrent HCC
- Thrombocytes 70x10log9; albumin 36 g/L; bilirubin 36 mcmol/L; INR 1,2;creatin 67 mcmol/L. CPA6/MELD11.
- Breakthrough telaprevir/peg/riba
- Treatment? Would you determine Q80K?

DAAs in HCV liver cirrhosis
Current situation

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SOF/DAC/riba	GT3	58-61%		High
3D/riba	GT1	92%/12w		High
		97%/24w		High

4. No time to waste or treat after liver transplantation ?

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DAAs in HCV liver cirrhosis
Data in decompensated cirrhosis scarce

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3D/riba	GT1	92%/12w		High
		97%/24w		High

See the forest for the trees

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ORIGINAL ARTICLE

Daclatasvir plus Sofosbuvir for Previously Treated or Untreated Chronic HCV Infection

Mark S. Sulkowski, M.D., David F. Gardiner, M.D., Maribel Rodriguez-Torres, M.D., K. Rajender Reddy, M.D., Tarek Hassanein, M.D., Ira Jacobson, M.D., Eric Lawitz, M.D., Anna S. Lok, M.D., Federico Hinestrosa, M.D., Paul J. Thuluvath, M.D., Howard Schwartz, M.D., David R. Nelson, M.D., Gregory T. Everson, M.D., Timothy Eley, Ph.D., Megan Wind-Rotolo, Ph.D., Shu-Pang Huang, Ph.D., Min Gao, Ph.D., Dennis Hernandez, Ph.D., Fiona McPhee, Ph.D., Diane Sherman, M.S., Robert Hindes, M.D., William Symonds, Pharm.D., Claudio Pasquinelli, M.D., Ph.D., and Dennis M. Grasela, Pharm.D., Ph.D., for the AI444040 Study Group

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ORIGINAL ARTICLE

Phase 2b Trial of Interferon-free Therapy for Hepatitis C Virus Genotype 1

Kris V. Kowdley, M.D., Eric Lawitz, M.D., Fred Poordad, M.D., Daniel E. Cohen, M.D., David R. Nelson, M.D., Stefan Zeuzem, M.D., Gregory T. Everson, M.D., Paul Kwo, M.D., Graham R. Foster, F.C.R.P., Mark S. Sulkowski, M.D., Wangang Xie, Ph.D., Tami Pilot-Matias, Ph.D., George Liossis, B.A., Lois Larsen, Ph.D., Amit Khatri, Ph.D., Thomas Podsadecki, M.D., and Barry Bernstein, M.D.

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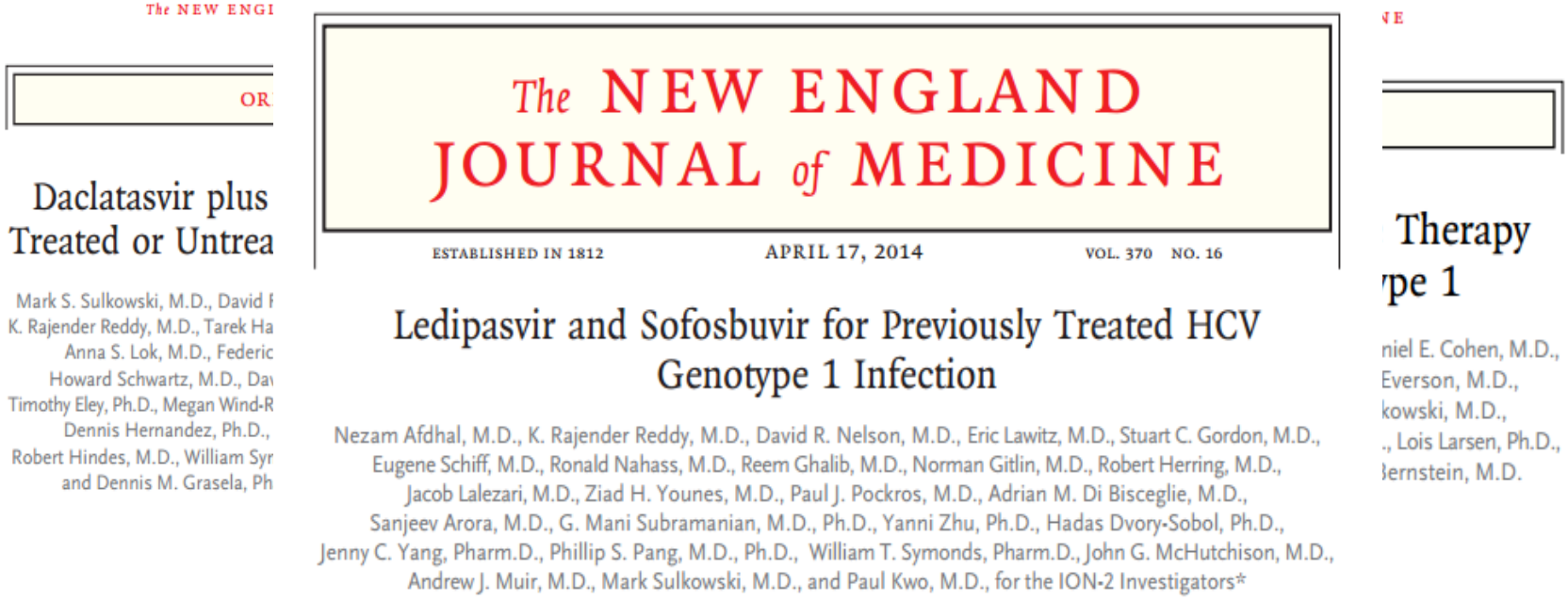

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Daclatasvir plus
Treated or Untrea

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Ledipasvir and Sofosbuvir for Previously Treated HCV Genotype 1 Infection

Nezam Afdhal, M.D., K. Rajender Reddy, M.D., David R. Nelson, M.D., Eric Lawitz, M.D., Stuart C. Gordon, M.D., Eugene Schiff, M.D., Ronald Nahass, M.D., Reem Ghalib, M.D., Norman Gitlin, M.D., Robert Herring, M.D., Jacob Lalezari, M.D., Ziad H. Younes, M.D., Paul J. Pockros, M.D., Adrian M. Di Bisceglie, M.D., Sanjeev Arora, M.D., G. Mani Subramanian, M.D., Ph.D., Yanni Zhu, Ph.D., Hadas Dvory-Sobol, Ph.D., Jenny C. Yang, Pharm.D., Phillip S. Pang, M.D., Ph.D., William T. Symonds, Pharm.D., John G. McHutchison, M.D., Andrew J. Muir, M.D., Mark Sulkowski, M.D., and Paul Kwo, M.D., for the ION-2 Investigators*

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., Lois Larsen, Ph.D.,
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Treatment of HCV with ABT-450/r–Ombitasvir and Dasabuvir with Ribavirin

Jordan J. Feld, M.D., M.P.H., Kris V. Kowdley, M.D., Eoin Coakley, M.D., Samuel Sigal, M.D., David R. Nelson, M.D., Darrell Crawford, M.D., Ola Weiland, M.D., Humberto Aguilar, M.D., Junyuan Xiong, M.S., Tami Pilot-Matias, Ph.D., Barbara DaSilva-Tillmann, M.D., Lois Larsen, Ph.D., Thomas Podsadecki, M.D., and Barry Bernstein, M.D.

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Retreatment of HCV with ABT-450/r–Ombitasvir and Dasabuvir with Ribavirin

Stefan Zeuzem, M.D., Ira M. Jacobson, M.D., Tolga Baykal, M.D., Rui T. Marinho, M.D., Ph.D., Fred Poordad, M.D., Marc Bourlière, M.D., Mark S. Sulkowski, M.D., Heiner Wedemeyer, M.D., Edward Tam, M.D., Paul Desmond, M.D., Donald M. Jensen, M.D., Adrian M. Di Bisceglie, M.D., Peter Varunok, M.D., Tarek Hassanein, M.D., Junyuan Xiong, M.S., Tami Pilot-Matias, Ph.D., Barbara DaSilva-Tillmann, M.D., Lois Larsen, Ph.D., Thomas Podsadecki, M.D., and Barry Bernstein, M.D.

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ABT-450/r–Ombitasvir and Dasabuvir with or without Ribavirin for HCV

Peter Ferenci, M.D., David Bernstein, M.D., Jacob Lalezari, M.D., Daniel Cohen, M.D., Yan Luo, M.D., Ph.D., Curtis Cooper, M.D., Edward Tam, M.D., Rui T. Marinho, M.D., Ph.D., Naoky Tsai, M.D., Anders Nyberg, M.D., Terry D. Box, M.D., Ziad Younes, M.D., Pedram Enayati, M.D., Sinikka Green, M.D., Yaacov Baruch, M.D., Bal Raj Bhandari, M.D., Florin Alexandru Caruntu, M.D., Ph.D., Thomas Sepe, M.D., Vladimir Chulanov, M.D., Ph.D., Ewa Janczewska, M.D., Ph.D., Giuliano Rizzardini, M.D., Judit Gervain, M.D., Ph.D., Ramon Planas, M.D., Christophe Moreno, M.D., Ph.D., Tarek Hassanein, M.D., Wangang Xie, Ph.D., Martin King, Ph.D., Thomas Podsadecki, M.D., and K. Rajender Reddy, M.D.

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Sofosbuvir and Ribavirin in HCV Genotypes 2 and 3

Stefan Zeuzem, M.D., Geoffrey M. Dusheiko, M.D., Riina Salupere, M.D., Ph.D., Alessandra Mangia, M.D., Robert Flisiak, M.D., Ph.D., Robert H. Hyland, D.Phil., Ari Illeperuma, M.S., Evguenia Svarovskaia, Ph.D., Diana M. Brainard, M.D., William T. Symonds, Pharm.D., G. Mani Subramanian, M.D., Ph.D., John G. McHutchison, M.D., Ola Weiland, M.D., Hendrik W. Reesink, M.D., Ph.D., Peter Ferenci, M.D., Christophe Hézode, M.D., and Rafael Esteban, M.D., for the VALENCE Investigators

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Ledipasvir and Sofosbuvir for 8 or 12 Weeks for Chronic HCV without Cirrhosis

Kris V. Kowdley, M.D., Stuart C. Gordon, M.D., K. Rajender Reddy, M.D., Lorenzo Rossaro, M.D.,
David E. Bernstein, M.D., Eric Lawitz, M.D., Mitchell L. Shiffman, M.D., Eugene Schiff, M.D., Reem Ghalib, M.D.,
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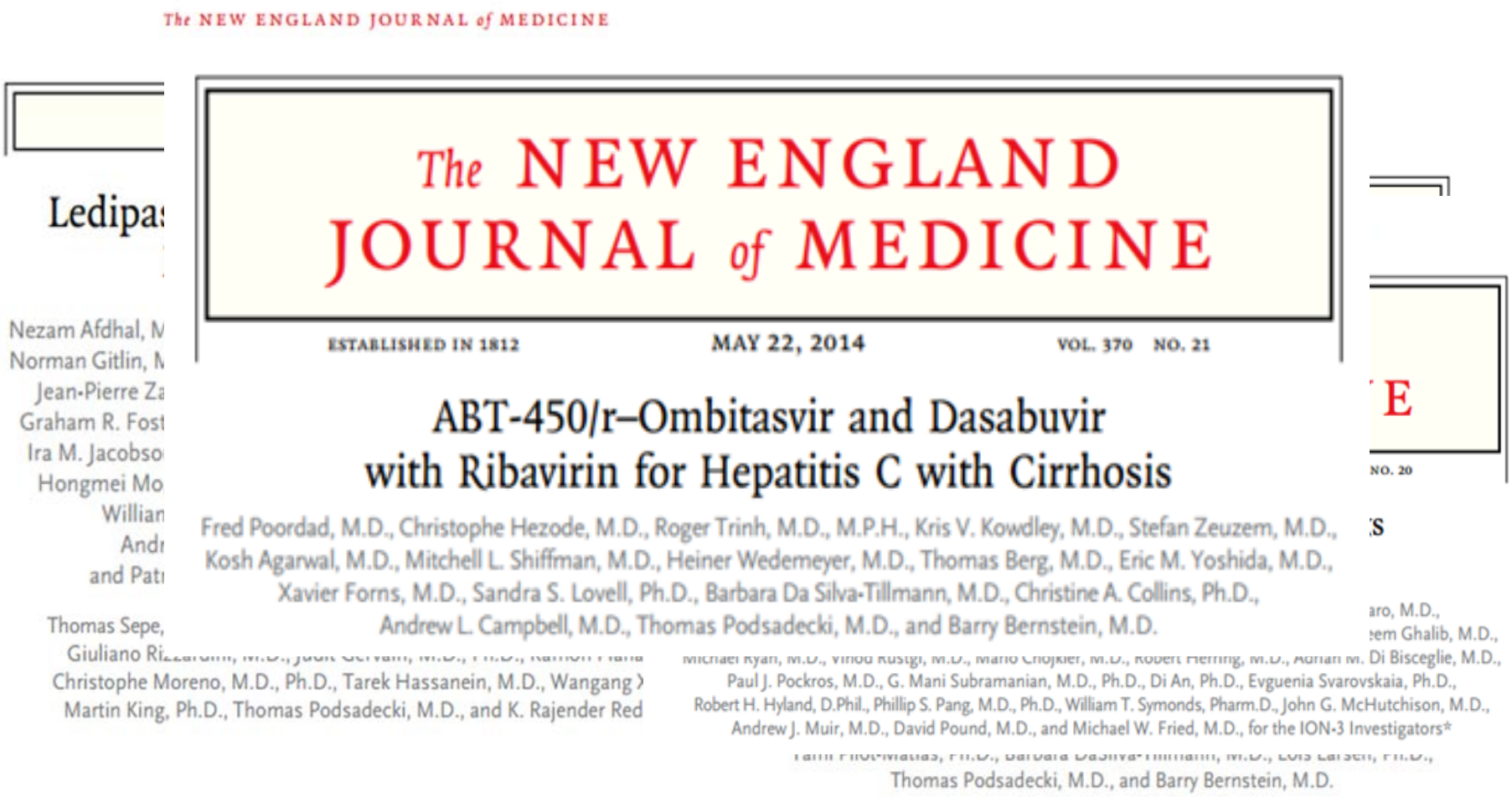

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Ledipas

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ABT-450/r–Ombitasvir and Dasabuvir with Ribavirin for Hepatitis C with Cirrhosis

Fred Poordad, M.D., Christophe Hezode, M.D., Roger Trinh, M.D., M.P.H., Kris V. Kowdley, M.D., Stefan Zeuzem, M.D., Kosh Agarwal, M.D., Mitchell L. Shiffman, M.D., Heiner Wedemeyer, M.D., Thomas Berg, M.D., Eric M. Yoshida, M.D., Xavier Forns, M.D., Sandra S. Lovell, Ph.D., Barbara Da Silva-Tillmann, M.D., Christine A. Collins, Ph.D., Andrew L. Campbell, M.D., Thomas Podsadecki, M.D., and Barry Bernstein, M.D.

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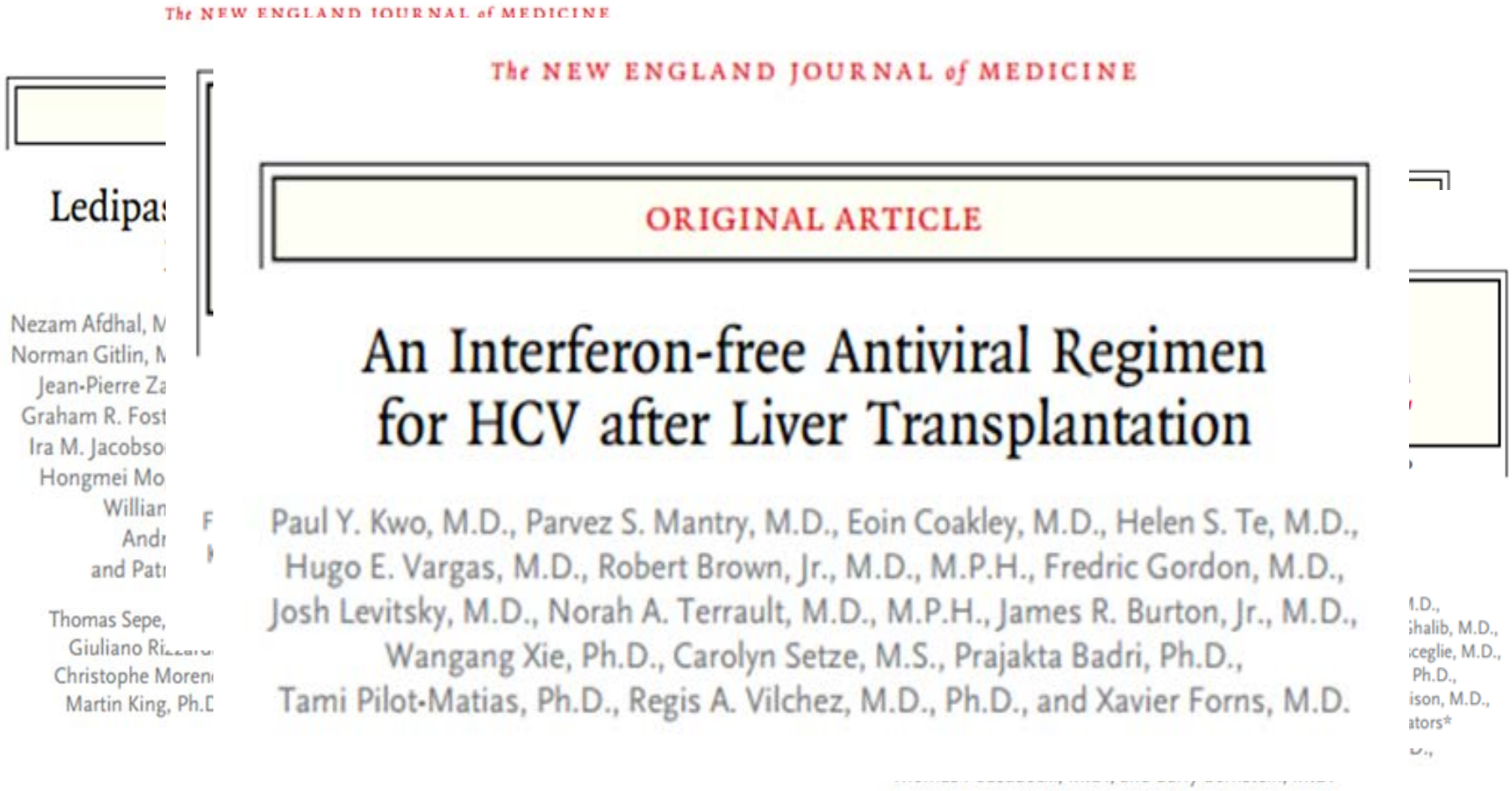

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ORIGINAL ARTICLE

An Interferon-free Antiviral Regimen for HCV after Liver Transplantation

Paul Y. Kwo, M.D., Parvez S. Mantry, M.D., Eoin Coakley, M.D., Helen S. Te, M.D., Hugo E. Vargas, M.D., Robert Brown, Jr., M.D., M.P.H., Fredric Gordon, M.D., Josh Levitsky, M.D., Norah A. Terrault, M.D., M.P.H., James R. Burton, Jr., M.D., Wangang Xie, Ph.D., Carolyn Setze, M.S., Prajakta Badri, Ph.D., Tami Pilot-Matias, Ph.D., Regis A. Vilchez, M.D., Ph.D., and Xavier Forns, M.D.

http://hcvsvrpredictor.liverdoc.com/#/
www.liverdoc.nl

BIBHEP: Tools facilitating treatment