

Clinical Performance of HBIG in Preventing Recurrent HBV After Liver Transplantation



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Introduction

- Orthotopic liver transplantation (OLT) remains the primary curative modality for end-stage liver disease from chronic hepatitis B (HBV) infection
- Initial attempts at OLT without immunoprophylaxis in this patient population resulted in over 80% re-infection of the allograft followed by accelerated graft failure

Introduction

- Extra-hepatic reservoirs of HBV, such as peripheral blood mononuclear cells and various organs, likely contributed to the high rate of re-infection
- These disappointing results caused many centers to abandon transplantation as a treatment option for chronic HBV infection in the late 1980s

HBIG Immunotherapy

- A review of domestic and international reports on combination therapy with HBIG and a nucleoside analog after OLT reveals consistent results
- Low recurrence rates up to 5 years post-transplant
- Data covers all HBV patients, including patients with high viral loads

Large Studies and Long-term Follow-up for HBIG Combination Therapy

Author	Location	# of Patients	Follow-up	Recurrences
Roche 2003	France	24	60 months	2 (8.3%)
Aribizu 2003	Spain	14	58.8 (15-107) months	1 (7%)*
Honaker 2002	Univ. of Tenn, USA	9	4.2 +/- 1.0 yr	0 (0%)
Dumortier 2003	France	17	30 (12-48) months	0 (0%)
Marzano 2001	Italy	26	29 +/- 9 months	1 (4%)
Engler 2002	Germany	5	26.6 (20-36) months	1 (20%)*
Rosenau 2001	Germany	21	643 (73-1473) days	4 (19%)
Angus 2000	Australia-New Zealand	37	18.4 +/- 12.1 (5-45) months	0 (0%)

*recurrence occurred after deviation from HBIG protocol

Alternatives

There are no good alternatives to HBIg for preventing recurrent HBV after OLT

Lamivudine Monotherapy

- Not a viable solution for all patients
- Routine development of escape mutants/drug resistance
- Historically 24-67% recurrence rate across all patients undergoing OLT for HBV

The UC Irvine Experience

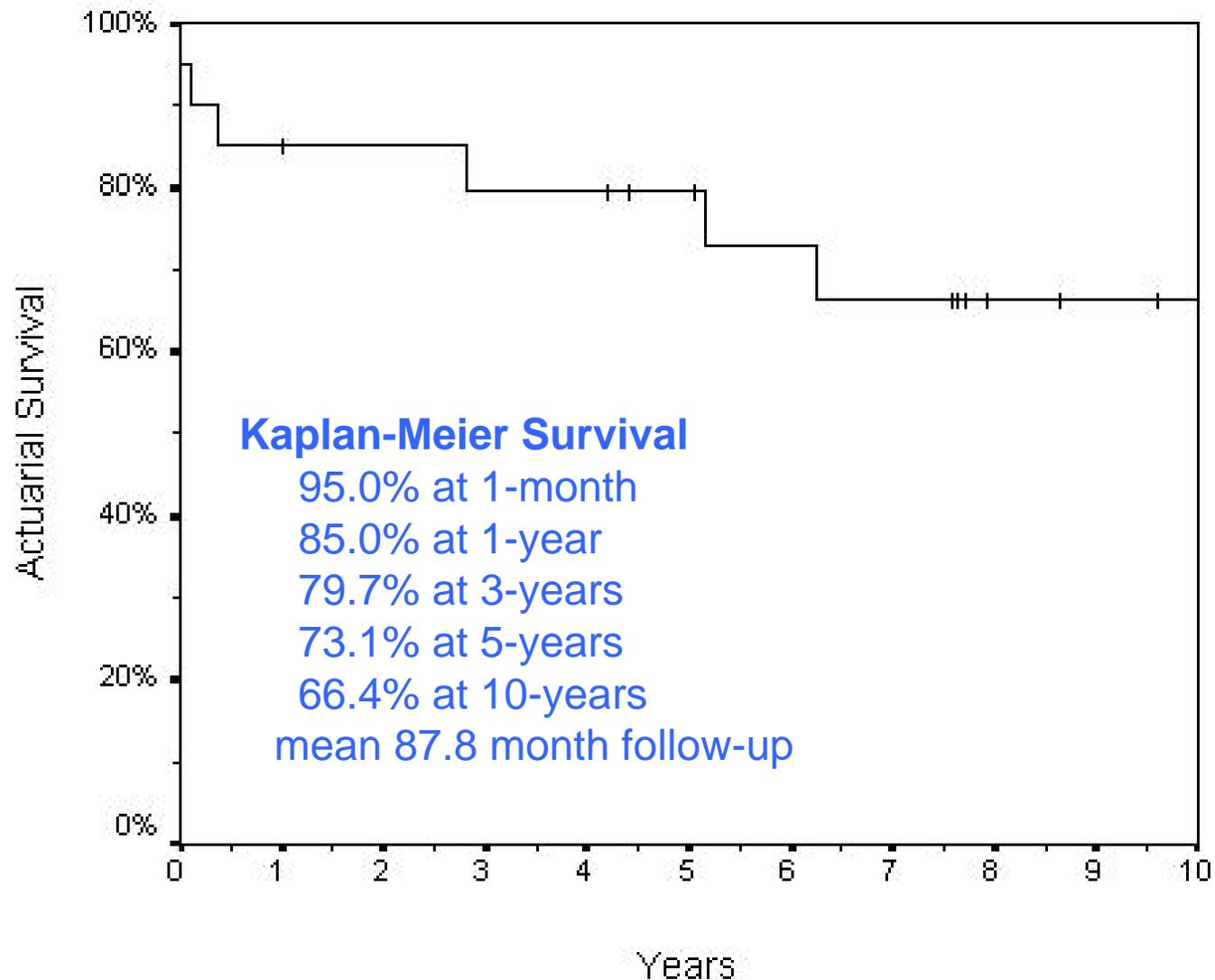
- Patients with HBV-related end-stage liver failure, followed at our institution
- Transplanted between 1993 and 2001 to ensure long-term follow up
- After OLT, all patients received combination therapy with HBIg and lamivudine

The UC Irvine Experience

HBIG Protocol

- During the anhepatic phase, 10,000 IU of HBIG was given intravenously (IV) followed by 10,000 IU of HBIG IV daily for 6 days
- Administration of HBIG was then changed to the intramuscular (IM) route and the frequency of doses was adjusted to maintain HBsAb titers above 150 IU/L
- Patients were evaluated on a monthly basis for the presence of HBV DNA and HBsAg until the HBsAb titers stabilized at therapeutic levels
- Thereafter, serology and HBsAb titers were checked every 2 months.

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Overall Results

# of Patients	# DNA + prior to OLT	Continued HBIg	Recurrent HBV	Follow-up months
10	2	Yes	0 (0%)	80.2 (range 34-115)
6	0	No	3 (50%)	100.6 (range 36.3-148.7)

The UC Irvine Experience

- 3 patients experienced recurrent HBV after cessation of HBIg and institution of lamivudine monotherapy
- Retrospectively, laboratory data demonstrates a marked increase in viral replication as HBsAb titers were depleted

Conclusions

- Published data strongly supports the use of combination therapy with HBIg and a nucleoside analog to prevent recurrent HBV after OLT
- There are no viable alternatives at this time

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