Secular Trends in the Etiologies and Outcomes of patients with Idiosyncratic DILI in the United States: Results from the DILIN Prospective study

Robert J. Fontana [1], Huiman Barnhart [2], Naga Chalasani [3], Paul B. Watkins [4], David E. Kleiner [5], Joseph A. Odin [6], Andrew Stolz [7], Victor Navarro [8], Jose Serrano [9], Sherry Gu [2] for the Drug Induced Liver Injury Network [1] Michigan Medicine, Ann Arbor, MI; [2] DCRI, Durham, NC; [3] Indiana University School of Medicine, Indianapolis, IN;; [4] University of North Carolina, Chapel Hill, NC; [5] National Cancer Institute, NIH, Bethesda, MD; [6] Icahn School of Medicine at Mount Sinai, New York, NY; [7] University of Southern California, Los Angeles, CA; [8] Einstein Health Systems, Philadelphia, PA; [9] NIDDK, NIH, Bethesda, MD.

AASLD The Liver Meeting® Nov. 12-15, 2021

DIGITAL EXPERIENCE

INTRODUCTION

The Drug Induced Liver Injury Network (DILIN) was established in 2004 to improve our understanding of the etiologies, risk factors and outcomes with idiosyncratic DILI in the United States.

To date, over 2200 adults and children have been enrolled into the DILIN Prospective Registry study.

AIM

To assess temporal trends in the clinical features, etiologies and outcomes of consecutively enrolled and adjudicated cases.

METHODS & RESULTS

Patients with DILI due to any drug or herbal and dietary supplement (HDS) are enrolled and followed for at least 6 months.

The clinical features, implicated drugs, and outcomes of high causality DILI cases scored as definite/ highly likely/ probable were compared by era of enrollment

Era 1 ='04-'09 Era 2= '10-'14 Era 3= '15-'20

1718 of the **2215 case** enrolled (77%) were adjudicated as high causality cases.

Data reported as median or %

RESULTS

Etiologies & outcomes by era

	Era 1 (517)	Era 2 (671)	Era 3 (530)	P trend
Age (yrs)	49.3	51.1	54.9	<0.001
Female	62%	55%	59%	0.07
Cau AA Asian Other	79.4% 10.1% 3.9% 6.6%	77.6% 14% 3.3% 5.1%	77.8% 13.1% 3% 6.1%	0.46
Mild-mod Mod-Hosp Severe Fatal	45% 27% 20% 8%	41% 34% 19% 6%	46% 33% 15% 6%	0.79 0.02 0.05 0.08
Antimicro HDS Cardiovas CNS Antineo Nitrofuran Isoniazid	50% 15% 10% 12% 5% 5% 6%	45% 24% 9% 6% 7% 4% 4%	44% 22% 6% 6% 11% 3% 2%	0.03 0.02 0.02 <0.001 <0.001 0.05 0.001
CLD	12%	7%	5%	<0.001
Steroids	23%	22%	22%	0.89
Liver bx	51%	46%	45%	0.10

Etiologies & outcomes by race

	White 1340	AA 215	Asian 58	Other 100	p
Age (yrs)	52.8	48.1	48.8	38.7	.001
Female	57%	66%	55%	57%	0.11
% HC	53%	55%	72%	64%	0.014
Peak ALT Peak Bili Peak INR	586 8.3 1.1	725 11.6 1.2	1040 12.9 1.2	798 11.3 1.2	0.001 0.003 .001
Mild Mod Mod-hos Severe Death/LT	26% 21% 30% 17% 6%	18% 14% 36% 22% 10%	15% 15% 41% 15% 12%	22% 12% 34% 23% 9%	< 0.001
Antimicro HDS Cardiovas Amox/Cla TMP/SMZ	44% 18% 8% 24% 8%	41% 16% 10% 15% 15%	50% 28% 5% 0% 11%	38% 36% 6% 12% 4%	0.47 <0.01 0.44 <0.01 0.14
Chronic	16%	23%	17%	5%	0.008
Steroids	21%	28%	17%	21%	0.09
CLD	8%	9%	9%	10%	0.79

Multivariate models of severe/ fatal outcome demonstrated that renal disease, AST, total bilirubin and albumin at onset were associated with poor outcomes These individuals were also significantly more likely to receive steroids and have DILI attributed to HDS products.

CONCLUSION

The implicated agents evolved over time with fewer cases due to antimicrobials (including nitrofurantoin and INH) and cardiovascular drugs but more due to HDS and anti-neoplastic agents.

Severity scores significantly improved over time with fewer needing LT or dying from DILI. The proportion with preexisting CLD also declined over time.

AA and Asian patients were more likely to present with HC injury, have DILI due to TMP/SMZ and HDS products and to experience severe/ fatal DILI.

In the overall cohort, renal disease and initial AST, bilirubin, and albumin levels were associated with greatest likelihood of death/ LT. HDS products were more frequently implicated in these cases and patients were more likely to receive steroid therapy.

ACKNOWLEDGEMENTS

This study was funded by the NIDDK U01/ U24 grants. See https:/dilin.org for funding sources and sites.

Clinical Trials.gov number: NCT00345930

CONTACT INFORMATION

Robert J. Fontana, MD

3912 Taubman Center, Ann Arbo

rfontana@med.umich.edu

Slides are the property of the author and AASLD. Permission is required from both AASLD and the author for reuse.