ID-week, Philadelphia, 8-12th October 2014

MATCH

Management of Post-Transplant Infections in Collaborating Hospitals

Elevation in Liver Transaminase (ALT-flares) in Transplant (TX) Recipients : Risk Factors and Consequences

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DISCLOSURES

NONE

MATCH
Management of Post-Transplant Infections in Collaborating Hospitals

BACKGROUND

- The Management of post Transplant infections in Collaborating Hospitals (MATCH) program was established in 2011 at Rigshospitalet, Copenhagen, Denmark
- MATCH aims to prevent infectious disease complications in the course of solid organ- (SOT) and hematopoietic stem-cell -transplantation (HSCT)
- One section of the MATCH program focuses on better understanding the clinical implications of liver injury in transplant recipients

BACKGROUND

- Destruction of hepatocytes → leakage of intracellular enzymes into the blood, incl alanine aminotransferase (ALT) → increases blood level of ALT → ALT-flare
- Caused by viral infections[1,2], other systemic infections[3], drug-induced-liver-injury (DILI)[4-6] and immunological reactions
- Risk factors, prognostic information, and possible causes of ALT-flares were poorly described in the literature for TX-recipients

HYPOTHESIS

ALT-flares in transplant recipients occur frequently and because of multiple reasons, but regardless of cause of flare and TX-type have negative impact on survival

[1]Cai J et al. Clin J Am Soc Nephrol 2012 Oct;7(10):1561-6.
[2]Gupta E et al, J Med Virol 2013 Mar;85(3):519-23.
[3]Daxboeck F et al Clin Microbiol Infect 2005 Jun;11(6):507-10.
[4]Sembera S, et al, Liver Transpl 2012 Jul;18(7):803-10.
[5]Vuppalanchi R et al. Pharmacol Ther 2010 Nov;32(9):1174-83.
[6]Verma S et al, Gut 2009 Nov;58(11):1555-64.
[6]Kim WR et al, Hepatology 2008 Apr;47(4):1363-70.

METHODS

Retrospective, grand-scale observational study

Patient cohort

- Solid Organ- (SOT) and Hematopoietic Stem-Cell Transplantation (HSCT) recipients
- All consecutively transplanted between September 2009 and June 2013 at our hospital
- Followed up from TX as routine care until either death, loss-to-follow-up (+ 60 days) or 22nd October 2013

ALT-flare

- Start of flare: ALT-value twice the minimum value and above 70 IU/ml
- Severity of flare: Maximum ALT value, above the upper limit of normal (ULN)

METHODS

Data collection

- MATCH database collate demographics, clinical variables, medicines used and results of biochemical/microbiological analysis (e.g. ALT measurements) determined as part of routine care
- For this analyses - patient chart reviewed of details around each ALT-flare (symptoms, diagnosis) and events preceding all observed deaths

Statistical analysis

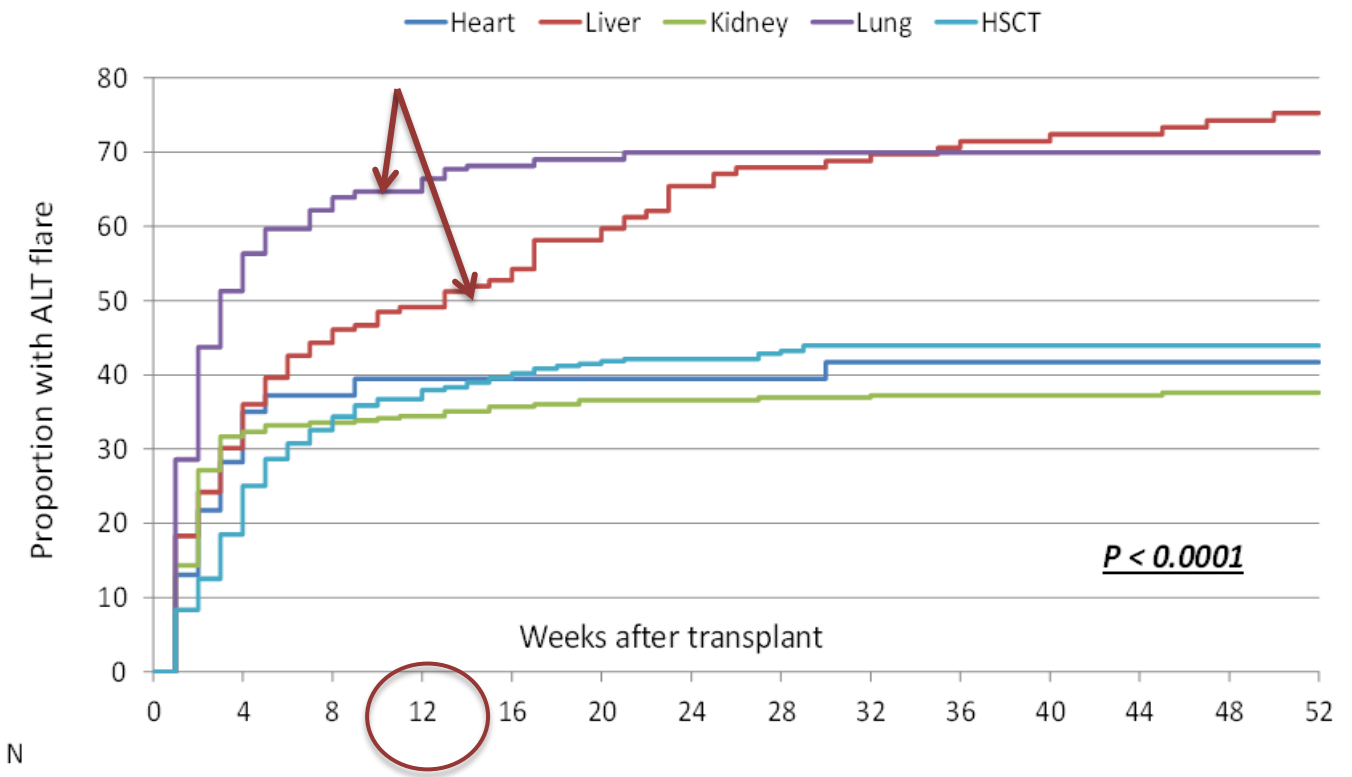
- Poisson regression for incidence rate ratio (IRR) of flare and death

RESULTS – characteristics of cohort

- **1002 transplant recipients**
  - SOT: 665
  - HSCT: 337
- **Follow-up**
  - 1937 person-years of FU
  - Median: 21.6 months (IQR: 10.8-34.8)
  - 153 died
- **ALT-flares post-tx**
  - Total #: 1220
  - Number of patients with
    - No flare: 500 (49.9%)
    - 1 flare: 230 (23.0%)
    - 2 flares: 113 (11.3%)
    - 3 or more flares: 159 (15.9%)

	Total	No ALT flare	1+ ALT flare
All	**1002**	500	502 (50.1%)
Heart	**47**	27	20 (42.6%)
Liver	**170**	50	120 (70.6%)
Kidney	**328**	200	128 (39.0%)
Lung	**120**	34	86 (71.7%)
HSCT	**337**	189	148 44.0%)

Time from transplantation to 1st flare



N					
Heart	47	29	27	27	25
Liver	170	108	74	41	23
Kidney	328	222	212	204	167
Lung	120	52	40	33	26
HSCT	337	250	198	168	116

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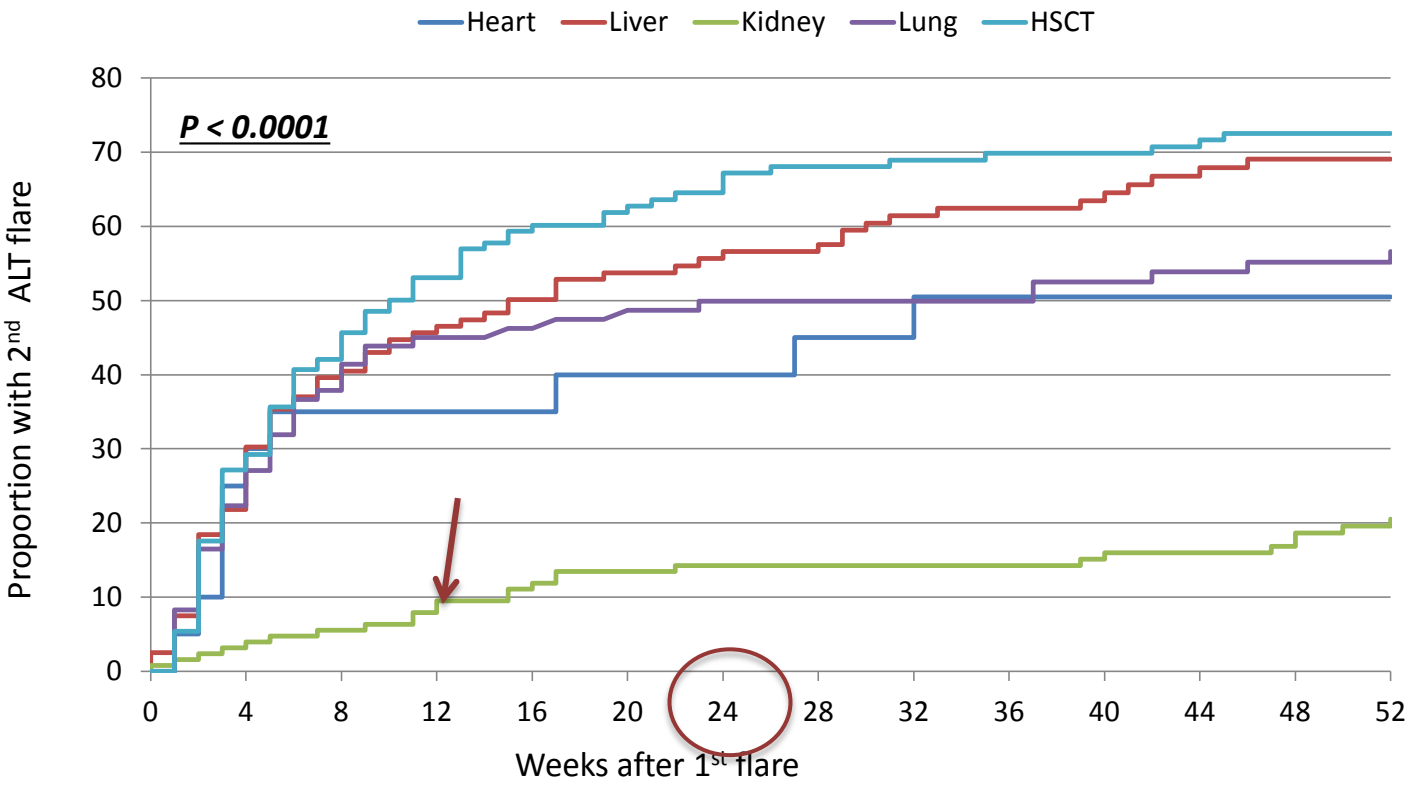
Time from 1st to 2nd flare



N					
Heart	20	14	13	12	9
Liver	117	82	60	46	25
Kidney	126	122	116	105	87
Lung	86	61	46	41	30
HSCT	144	100	62	40	25

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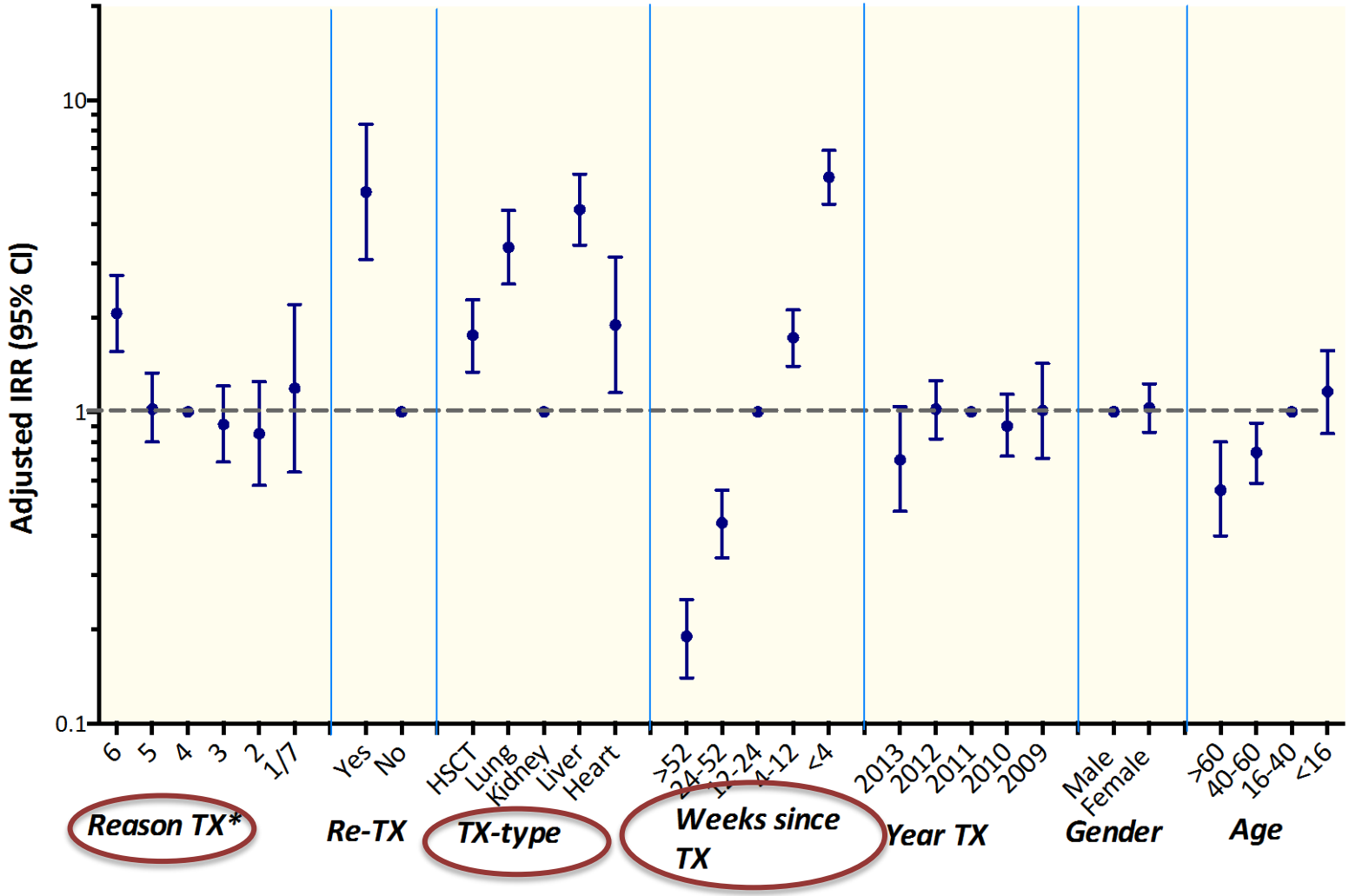
Factors associated with flare development / adjusted model



*Factors adjusted for in the model: Age, Gender, Year TX, Weeks since TX, TX-type, Re-TX, Reason TX**

** 1=reduced perfusion, 2=acute insufficiency/organ failure, 3=chronic organ failure, 4=reduced function due to chronic impact, 5=autoimmune/hereditary disease, 6=malignancy, 7=unknown/unreported.*

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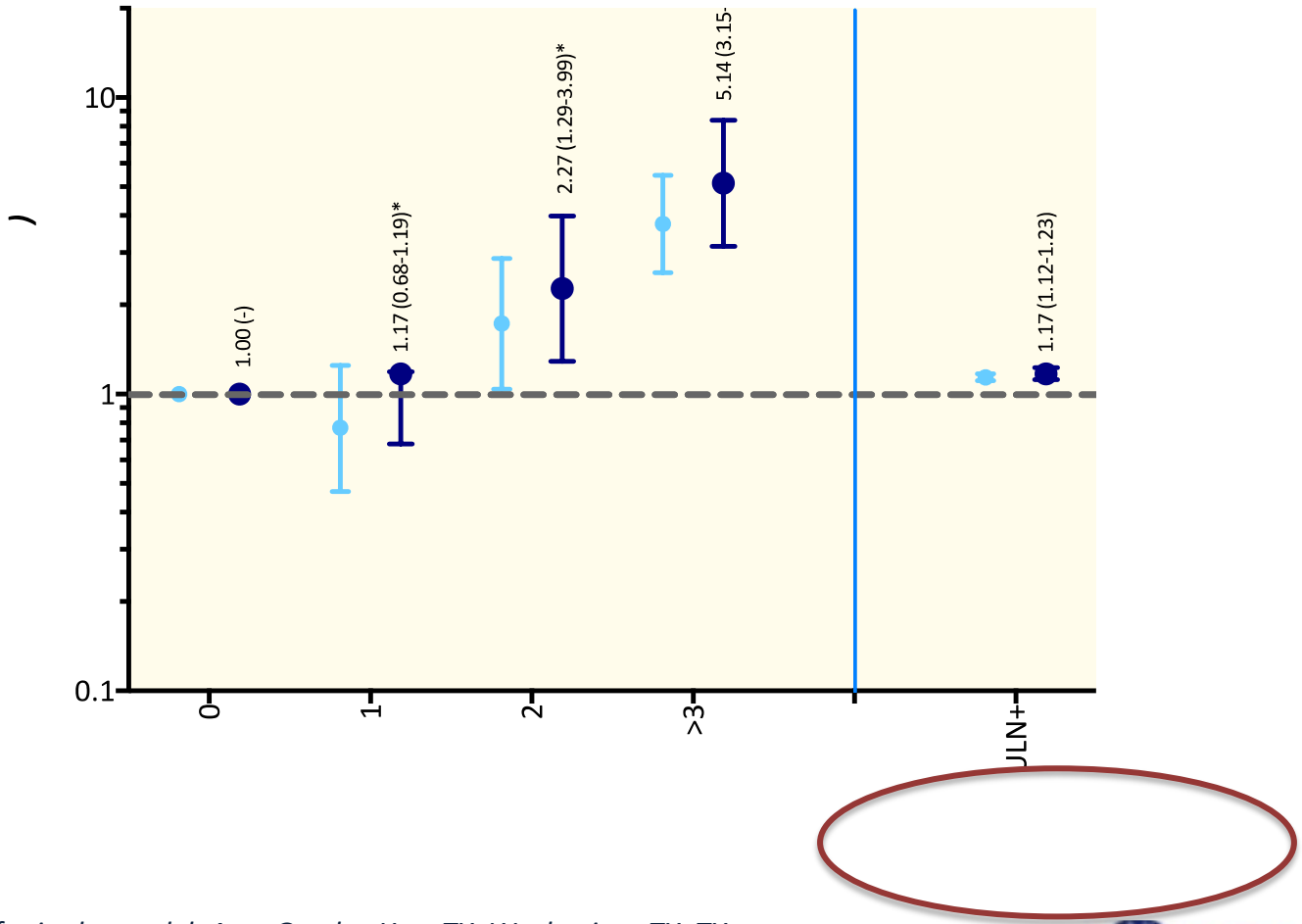
Risk of death associated with number and severity of ALT-flares



**Factors adjusted for in the model: Age, Gender, Year TX, Weeks since TX, TX-type, Re-TX, Reason TX, number of flares and ULN+ of flare (pr. 5 IU/ml)*

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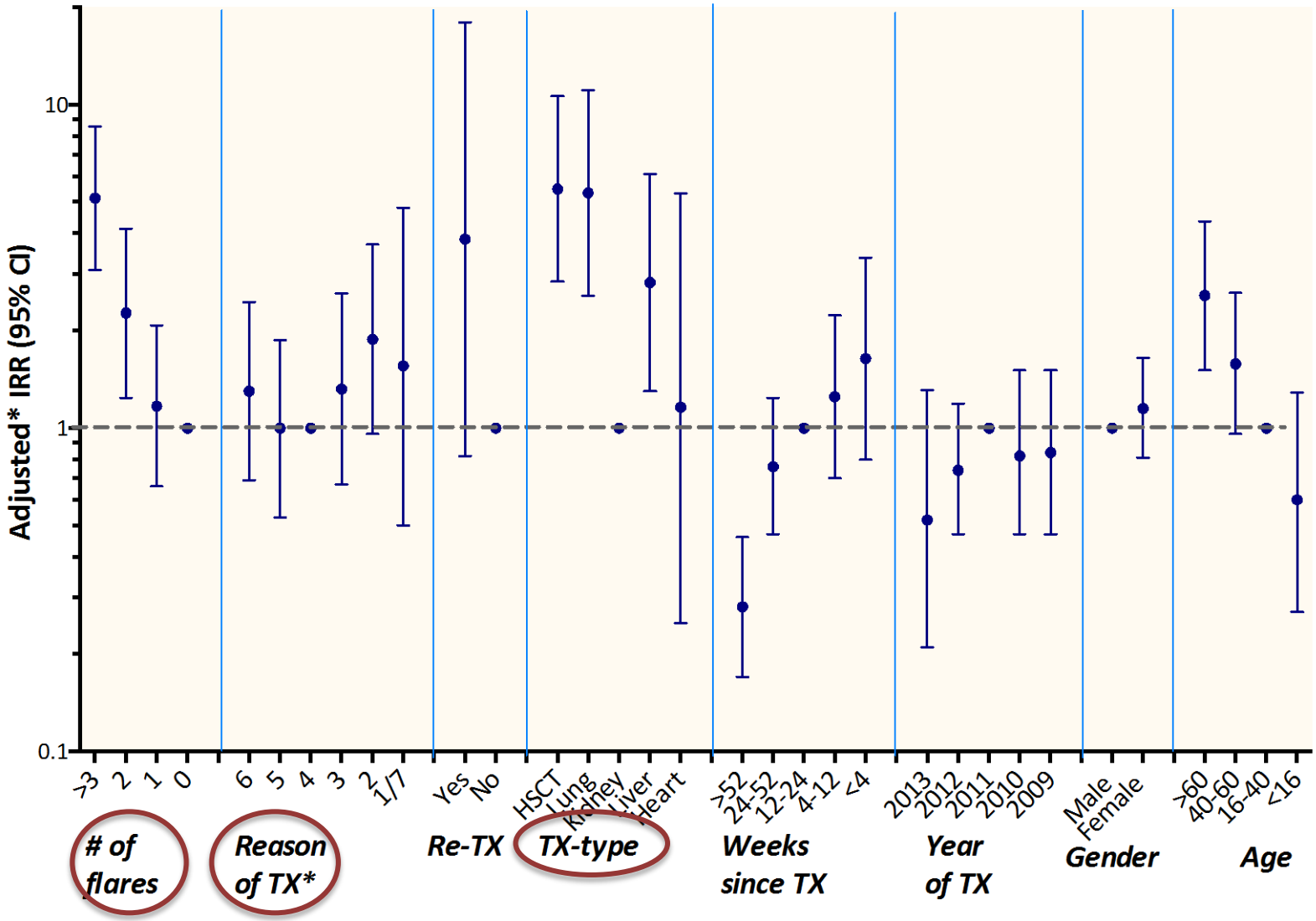
Other factors associated with death



Factors adjusted for in the model: Age, Gender, Year TX, Weeks since TX, TX-type, Re-TX, Reason TX and number of flares*

** 1=reduced perfusion, 2=acute insufficiency/organ failure, 3=chronic organ failure, 4=reduced function due to chronic impact, 5=autoimmune/hereditary disease, 6=malignancy, 7=unknown/unreported.*

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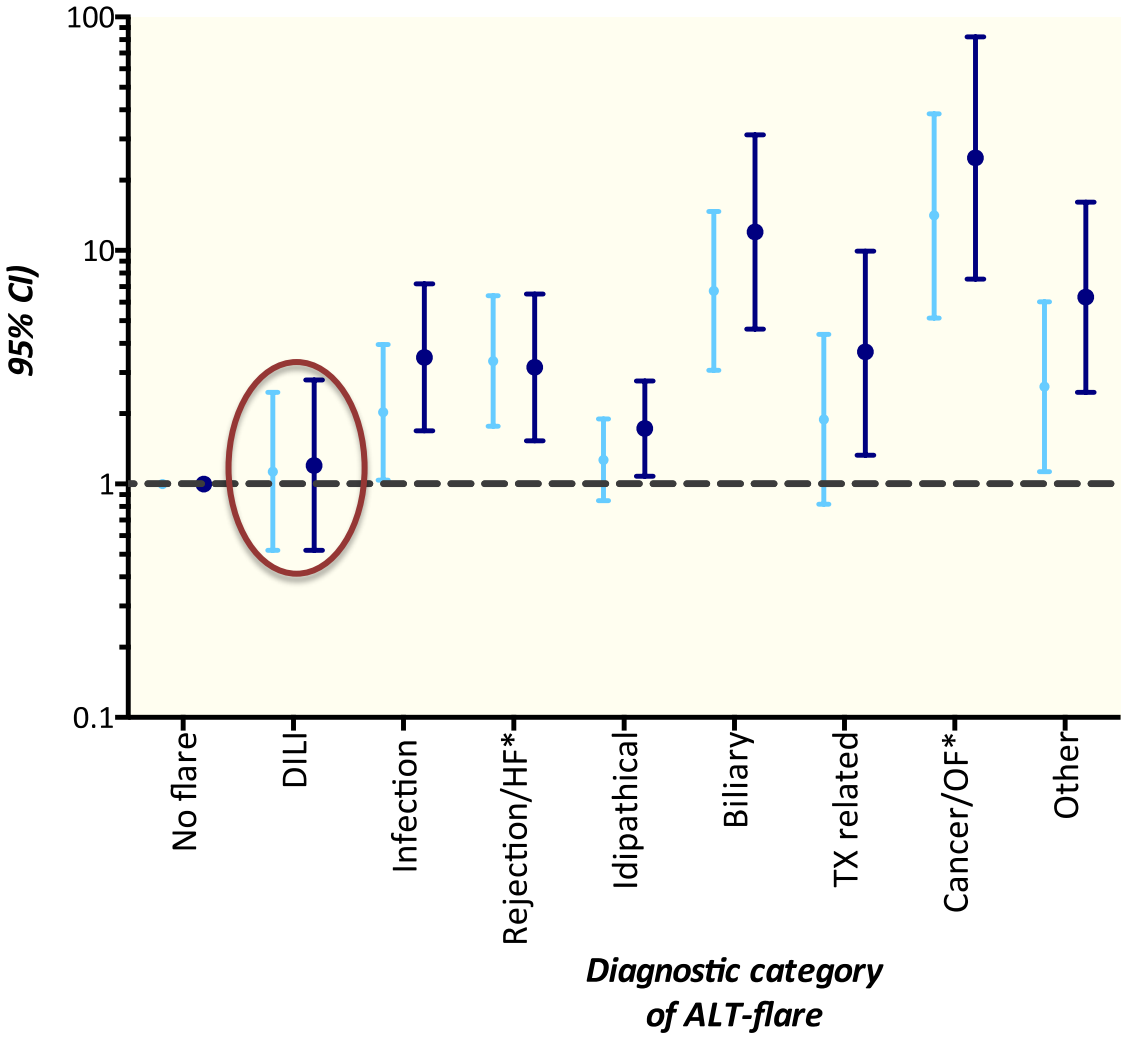
Type of flare and association w. death



*HF=Heart Failure, OF=Organ Failure
**Factors adjusted for in the model: Age, Gender, Year TX, Weeks since TX, TX-type, Re-TX, Reason TX* and number of flares
Other: Biliary (7 deaths), TX-related (6 deaths), cancer/OF (4 deaths) and other (6 deaths)

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Limitations/strength

LIMITATIONS

- Unable to access all specific types of medicines the recipients received.
- Observational studies are unable to determine causal links → rational basis for more focused studies

STRENGTHS

- The large patient cohort
- The diverse characteristics of the cohort, including all different transplantation types → universally applicable
- Great and detailed amounts of data on diverse clinical variables

CONCLUSION

- ALT-flares occurs frequently during the course of transplantation
- Several ALT-flares, in particular if severe, are major prognostic factors of mortality, irrespective of type of transplantation
- Future studies should examine potential biological mechanisms explaining the association

QUESTIONS?

THANK YOU

IDSA

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