Dr Anthony Mato - Disclosures

- Research
  - TG Therapeutics
  - Pharmacyclics
  - Abbvie
  - Johnson and Johnson
  - Acerta / AZ
  - Regeneron
  - DTRM BioPharma
  - Sunesis
  - Loxo
- Advisory / Consultancy
  - TG Therapeutics
  - Pharmacyclics
  - Abbvie
  - Johnson and Johnson
  - Acerta / AZ
  - DTRM BioPharma
  - Sunesis
  - Celgene
  - Verastem

Predicting tumor lysis syndrome (TLS) in venetoclax-treated CLL patients

Objectives

1. To describe **rates of TLS** observed in **clinical practice** and clinical trial settings
2. To understand factors at baseline that may **improve prediction of TLS events** in addition to ALC and lymph node size.

Materials and Methods

- **Design:** Multicenter, retrospective cohort study of 339 CLL pts treated with venetoclax
- **Data:** Collected demographics, baseline characteristics, TLS risk and prophylaxis, and TLS occurrence (Howard criteria)
- **Analysis:** Test association between risk factors and TLS development (OR estimated with univariable logistic regression)
- **Model:** Multivariable logistic regression of statistically significant ($p<0.05$) predictors of TLS was performed. Calculated area under the receiver operator characteristic curve for the model including independent predictors of TLS

Baseline Characteristics

Total Cohort n=339	
Age, median (range)	67 (37-91)
Male	69%
Race, White	85%
Ven monotherapy	79%
Ven on clinical trial	13%
R/R	94%
Unmutated IGHV	84% (n=118)
del(17p)	43% (n=323)
Complex karyotype	39% (n=213)
Prior lines of therapy, median (range)	3 (0-15)
Prior ibrutinib	78% (n=319)

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TLS risk, prophylaxis and rates
Univariable analysis of TLS development risk

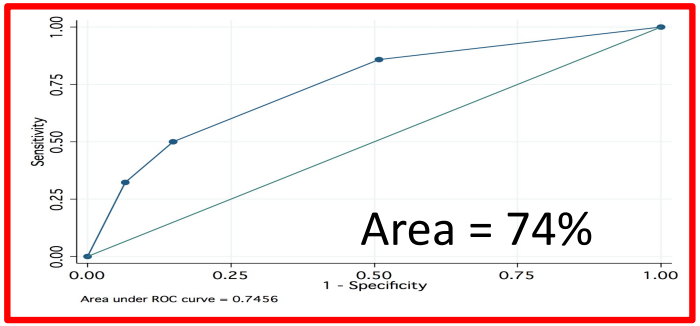
TLS Risk Stratification	
Low TLS Risk	38%
Intermediate TLS Risk	34%
High TLS Risk	28%
CrCl < 80 mL/min	45%
Imaging performed	94%
TLS Prophylaxis Strategies	
Allopurinol	93% (n=206)
Rasburicase	43% (n=307)
Normal Saline	87% (n=204)
Planned hospitalization, med (range)	2 (0-5)
≥1 planned hospitalization	75%
TLS Rates	
Overall TLS rate	10% (35/339)
Clinical TLS	9 cases
Lab TLS	26 cases

Univariable Analysis	Odds Ratio	p Value
Sex (female vs. male)	1.2	0.62
Creatinine clearance (≤80 vs >80 mL/min)	**2.9**	**0.015**
Complex karyotype	**2.2**	**0.04**
del(17p)	0.93	0.84
IGHV unmutated	0.76	0.74
Prior ibrutinib exposure	0.74	0.48
Venetoclax administration (monotherapy vs. combo)	2.9	0.09
TLS risk		
medium vs. low	2.4	0.09
high vs. low	**4.2**	**0.004**
high vs. low + medium	**2.6**	**0.01**

Multivariable analysis of risk of TLS development and conclusions

Multivariable Analysis	Odds Ratio	95% C.I.	p value
TLS Risk (high vs. low + medium)	**5.87**	**(2.42, 14.3)**	**<0.001**
Creatinine Clearance (<80 vs. ≥80 mL/min)	**2.53**	**(1.03, 6.25)**	**0.044**
Complex karyotype (present vs. absent)	2.36	(0.98, 5.70)	0.055

ROC curve of multivariate model including TLS risk group (high vs. low + medium) and creatinine clearance (< 80 mL/min vs. ≥ 80 mL/min), **area under the ROC curve is 74.6%.**



Conclusions

- **Renal function matters:** Patients with impaired renal function (creatinine clearance < 80 mL/min) are at **increased risk of TLS independent of tumor burden**
- Further study of **creatinine clearance as a continuous variable to refine risk** is warranted and future models of TLS risk stratification should consider incorporation of renal function
- Practitioners **may consider modifying prophylaxis and monitoring** strategies **based on renal function** to decrease observed rates of TLS
- Complex karyotype did not reach statistical significance as a predictor of TLS, though further study in larger series is warranted

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