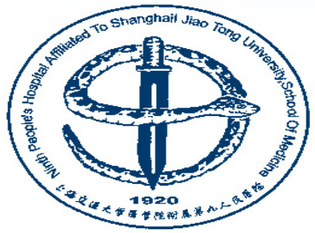
2020 AHA SOLOIST-WHF Study

上海交通大学医学院附属第九人民医院心内科

范虞琪



上海交通大學 医学院附属第九人民医院

Shanghai Ninth People's Hospital affiliated to Shanghai JiaoTong University, School of Medicine

Daily Recap and LBS.07

SOLOIST

Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure – The SOLOIST-WHF Trial

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#AHA20

研究方法

- 三期、双盲、随机、安慰剂对照试验。
- 患者以1:1随机分配至索格列净组和对照组，索格列净组患者每天接受200mg索格列净治疗，对照组患者接受安慰剂治疗。
- 主要纳入标准为
  1）2型糖尿病；
  2）18-85岁；
  3）因心衰住院且接受利尿剂治疗。

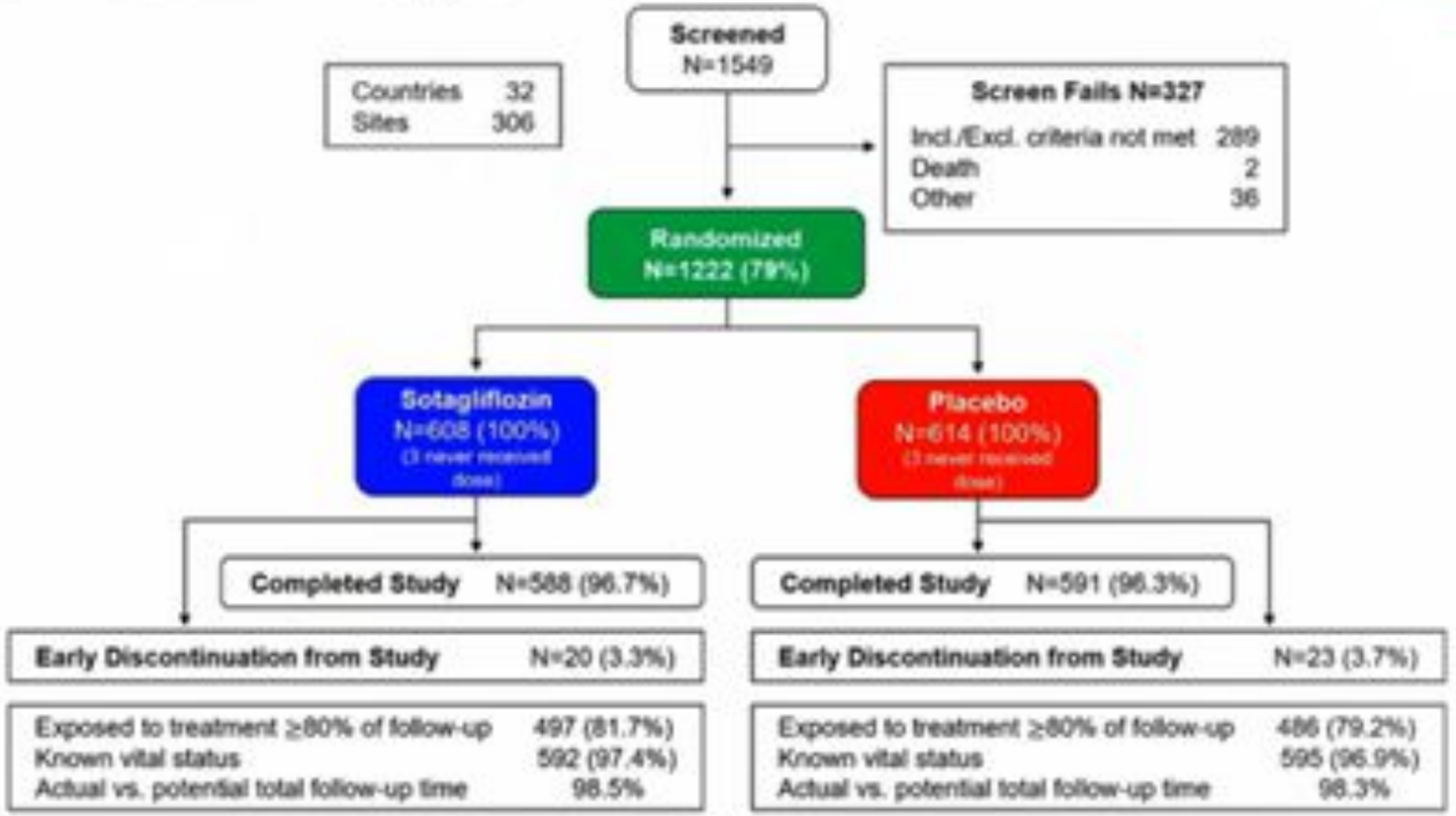
研究方法

- 主要排除标准为
  - 不需要氧疗，收缩压≥100 mmHg，
  - 不需要静脉应用正性肌力药物或血管扩张剂，以及由静脉利尿剂转为口服利尿剂。
  - 患者的BNP升高＞150pg/ml（房颤患者＞450pg/ml），NT-proBNP＞600pg/ml（房颤患者＞1800pg/ml）。

- 在随机后的1、2、4周进行随访，之后每4个月随访一次。

CONSORT Diagram

SOLOIST



研究设计

- 主要终点为心源性死亡、因心力衰竭住院和急诊就诊的总人数。
- 次要终点事件包括因心衰住院或急诊就诊的总人数，心源性死亡的发生率，全因死亡的发生率，心源性死亡、因心衰住院、非致死性心肌梗死和非致死性卒中的总人数，因心源性死亡、因心衰住院和紧急就诊的总人数，以及住院期间发生的心力衰竭事件的总人数；堪萨斯市心肌病问卷12项得分变化以及GFR的变化。

研究结果 （baseline）

- 1222名患者，608名索格列净+614名患者对照组，
- 中位年龄为70岁，33.7%为女性，93.2%为白人。
- 79.1%的患者LVEF＜50%，中位GFR为49.7 ml / min / 1.73 m2，
- 中位糖化血红蛋白水平为7.1%
- 中位NT-proBNP水平为1799.7pg/ml。

研究结果

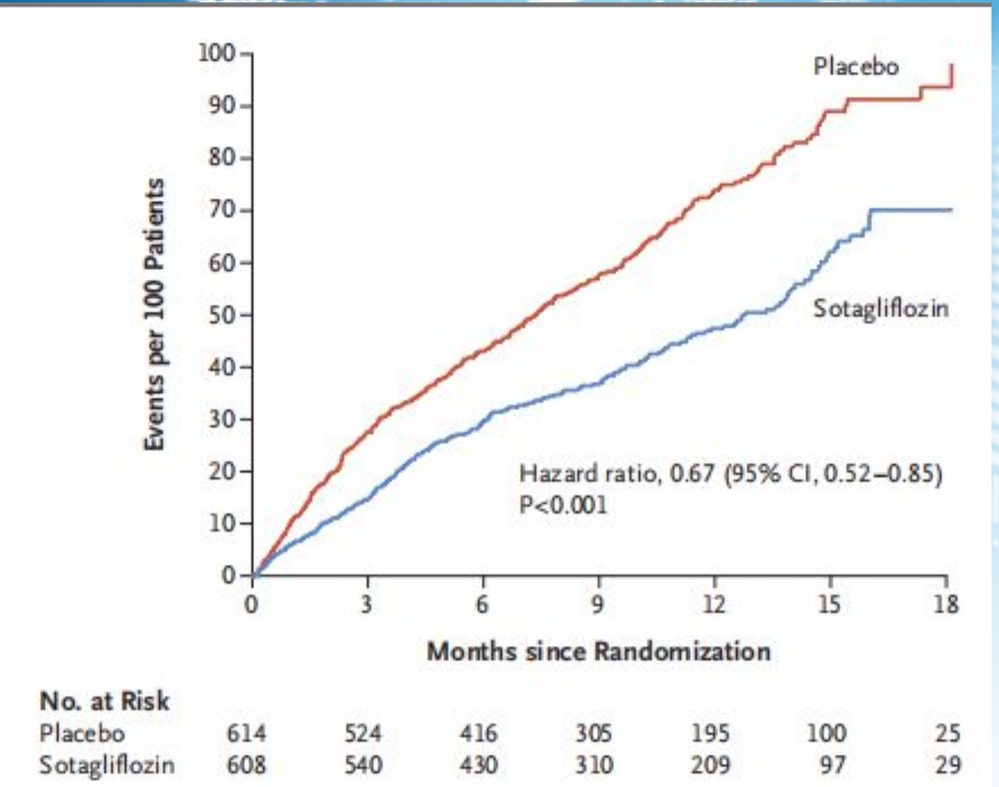


Figure 1. Primary Efficacy End-Point Events.

Shown are the rates of primary efficacy end-point events (deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure) in the sotagliflozin group and the placebo group. Total events after randomization are shown as estimated cumulative events per 100 patients instead of events per 100 patient-years to graphically show the time course of event accrual during follow-up. Competing deaths from noncardiovascular causes occurred in 14 patients in the sotagliflozin group and in 18 patients in the placebo group.

- 1222例患者中共发生了600例主要终点事件（索格列净组245例，安慰剂组355例）。
- 索格列净组的主要终点事件发生率为51.0/100名患者*年，安慰剂组为76.3/100名患者*年（HR:0.67; 95%CI 0.52～0.85; p< 0.001），绝对差异为每100名患者年发生25.3起事件（95%CI: 5.1-45.6）。

亚组分析研究结果

Subgroup	No. of Patients	Sotagliflozin	Placebo	Hazard Ratio (95% CI)
		events per 100 patient-yr		
Overall	1222	51.0	76.3	0.67 (0.52–0.85)
LVEF				
<50%	966	56.9	79.9	0.72 (0.56–0.94)
≥50%	256	30.6	64.0	0.48 (0.27–0.86)
Geographic region				
North America or Latin America	346	68.3	103.0	0.64 (0.43–0.95)
Europe	800	44.1	64.7	0.69 (0.50–0.95)
Rest of the world	76	48.4	78.3	0.60 (0.23–1.58)
Timing of first dose				
Before discharge	596	52.1	76.6	0.71 (0.51–0.99)
After discharge	626	50.0	76.1	0.64 (0.45–0.90)
Sex				
Female	412	41.9	52.0	0.80 (0.51–1.25)
Male	810	55.7	89.3	0.62 (0.47–0.82)
Age				
<65 yr	364	57.1	71.1	0.79 (0.51–1.23)
≥65 yr	858	48.0	78.5	0.62 (0.47–0.82)
Estimated GFR				
<60 ml/min/1.73 m²	854	50.1	85.8	0.59 (0.44–0.79)
≥60 ml/min/1.73 m²	368	53.1	58.1	0.90 (0.58–1.37)

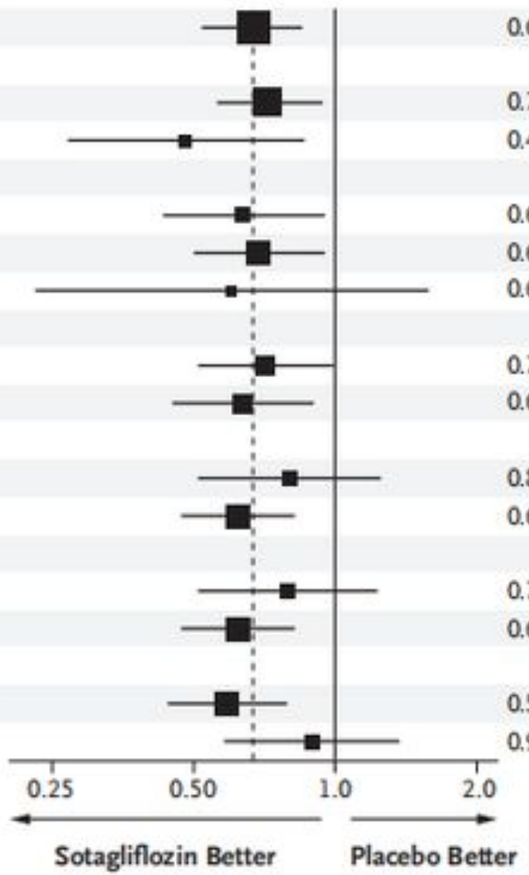


Figure 2. Primary Efficacy End-Point Events in Select Prespecified Subgroups.

Shown are the hazard ratios with 95% confidence intervals for primary end-point events in select prespecified subgroups. The confidence intervals have not been adjusted for multiple testing, and inferences drawn from the intervals may not be reproducible. Left ventricular ejection fraction (LVEF) was categorized according to the randomization stratification factor. GFR denotes glomerular filtration rate.

人民医院
School of Medicine

研究结果

Table 2. Primary End Point and Secondary End Points.

End Point	Sotagliflozin (N=608)	Placebo (N=614)	Hazard Ratio or Difference (95% CI)*	P Value
Primary end point: deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure — total no. of events (rate)†	245 (51.0)	355 (76.3)	0.67 (0.52 to 0.85)	<0.001
Secondary end points in order of hierarchical testing				
Hospitalizations and urgent visits for heart failure — total no. of events (rate)†	194 (40.4)	297 (63.9)	0.64 (0.49 to 0.83)	<0.001
Deaths from cardiovascular causes — total no. of events (rate)†	51 (10.6)	58 (12.5)	0.84 (0.58 to 1.22)	0.36‡
Deaths from cardiovascular causes, hospitalizations for heart failure, nonfatal myocardial infarctions, and nonfatal strokes — total no. of events (rate)†	247 (51.4)	330 (71.0)	0.72 (0.56 to 0.92)	
Deaths from cardiovascular causes, hospitalizations and urgent visits for heart failure, and events of heart failure during hospitalization — total no. of events (rate)†	263 (54.7)	375 (80.6)	0.68 (0.54 to 0.86)	
Deaths from any cause — total no. of events (rate)†	65 (13.5)	76 (16.3)	0.82 (0.59 to 1.14)	
Least-squares mean change in KCCQ-12 score to month 4	17.7	13.6	4.1 (1.3 to 7.0)	
Least-squares mean change in estimated GFR — ml/min/1.73 m^2	−0.34	−0.18	−0.16 (−1.30 to 0.98)	

* Hazard ratios (sotagliflozin vs. placebo) are shown for all end points except change in KCCQ-12 score to month 4 and change in estimated GFR, for which differences in the least-squares mean values are shown (sotagliflozin minus placebo).
† Rate was calculated as the number of events per 100 person-years of follow-up.
‡ The hierarchical analysis was stopped after the first P value indicating nonsignificance.

第一次要终点分析的结果（因心衰住院和急诊就诊的总人数）与主要终点分析的结果一致。因心血管原因或全因死亡的发生率在两组之间无显著差异。其他各项终点虽有减少事件发生的趋势，但是均无统计学差异

安全性研究结果

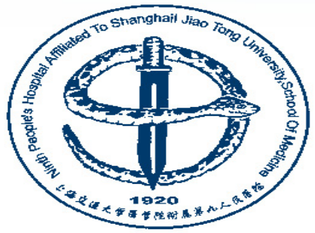
- 在索格列净或安慰剂组分别有3.0%和2.8%的患者因严重不良事件而停药。
- 除心力衰竭外，索格列净组和安慰剂组最常见的不良事件为低血压（6.0% vs. 4.6%）、尿路感染（4.8% vs. 5.1%）和腹泻（6.1% vs. 3.4%）。
- 索格列净组和安慰剂组分别有4.1%和4.4%的患者发生了急性肾损伤。
- 严重低血糖在索格列净组比安慰剂组更常见（1.5% vs. 0.3%）。

结论

- 在心衰失代偿性发作的2型糖尿病患者中，在出院前或出院后不久开始索格列净治疗，可以减少心血管死亡及因心力衰竭住院或紧急就诊的发生。

- 在亚组分析中我们注意到无论对于射血分数保留的心衰（HFpEF）还是射血分数降低的心衰（HFrEF），应用索格列净均可减少终点事件的发生，但是在HFpEF患者中效果更好（HR：0.48 vs 0.72），也为HFpEF治疗提供了新的思路。

谢 谢



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