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Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness:

A Randomized Clinical Trial

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Abstract

IMPORTANCE—For patients with limited prognosis, some medication risks may outweigh the benefits, particularly when benefits take years to accrue; statins are one example. Data are lacking regarding the risks and benefits of discontinuing statin therapy for patients with limited life

OBJECTIVE-To evaluate the safety, clinical, and cost impact of discontinuing statin medications for patients in the palliative care setting.

DESIGN, SETTING, AND PARTICIPANTS—This was a multicenter, parallel-group, unblinded, pragmatic clinical trial. Eligibility included adults with an estimated life expectancy of between 1 month and 1 year, statin therapy for 3 months or more for primary or secondary prevention of cardiovascular disease, recent deterioration in functional status, and no recent active cardiovascular disease. Participants were randomized to either discontinue or continue statin therapy and were monitored monthly for up to 1 year. The study was conducted from June 3, 2011, to May 2, 2013. All analyses were performed using an intent-to-treat approach.

INTERVENTIONS—Statin therapy was withdrawn from eligible patients who were randomized to the discontinuation group. Patients in the continuation group continued to receive statins.

MAIN OUTCOMES AND MEASURES—Outcomes included death within 60 days (primary outcome), survival, cardiovascular events, performance status, quality of life (QOL), symptoms, number of nonstatin medications, and cost savings.

RESULTS—A total of 381 patients were enrolled; 189 of these were randomized to discontinue statins, and 192 were randomized to continue therapy. Mean (SD) age was 74.1 (11.6) years, 22.0% of the participants were cognitively impaired, and 48.8% had cancer. The proportion of participants in the discontinuation vs continuation groups who died within 60 days was not significantly different (23.8% vs 20.3%; 90% CI, -3.5% to 10.5%; P=.36) and did not meet the noninferiority end point. Total QOL was better for the group discontinuing statin therapy (mean McGill QOL score, 7.11 vs 6.85; P = .04). Few participants experienced cardiovascular events (13 in the discontinuation group vs 11 in the continuation group). Mean cost savings were \$3.37 per day and \$716 per patient.

CONCLUSIONS AND RELEVANCE—This pragmatic trial suggests that stopping statin medication therapy is safe and may be associated with benefits including improved QOL, use of fewer nonstatin medications, and a corresponding reduction in medication costs. Thoughtful patient-provider discussions regarding the uncertain benefit and potential decrement in QOL associated with statin continuation in this setting are warranted.

_	Nr. (%)				
Varjable .	Diseastinued Statin (n = 187)	Continued Statin (n = 192)	Tatal (N = 3\$1)	P Valor	
Age, mean (SU), y	74.8 (11 7)	73.5 (11.5)	74.1 (11.6)	.29	
Sex					
Male	98 (51 9)	112 (59 3)	210 (55 1)	- "2u	
Femele	9) (4k.t)	80 (41 P)	171 (44 9)		
Ince					
W/hte	153 (81 6)	162 (#4.4)	315 (82.7)		
lilack	52 (16 9)	22 (11 5)	51 (14.2)	30	
Other	3 (1 6)	7(36)	16 (2.5)		
Multiple	1 (0.5)	1 (0.5)	2 (0.5)		
Ethnically					
Hasponic	6 (3.2)	20 (5.2)	16 (4.2)	-	
Non-Haspanic	182 (96 3)	iki (943)	363 (95 3)	.32	
Unknown	1(05)	i (ü.≸j	2 (0 5)		
Educational level					
<high school<="" td=""><td>27 (14.3)</td><td>24 (12.5)</td><td>51 (L3 4)</td><td>_</td></high>	27 (14.3)	24 (12.5)	51 (L3 4)	_	
High school graduate	100 (52 9)	95 (49.5)	195 (51.2)	- A3	
College graduate	61 (32.3)	70 (16.5)	131 (34.4)		
L'aluntren	1 (0.5)	3 (1 4)	4 (L D)		
Insurance					
Medicare	140 (74 1)	140 (72 9)	280 (73.5)	_	
Medicard	18 (9,5)	JA (K.3)	34 (8 9)		
Private	23 (12.2)	20 (1 4)	43 (11 3)	_ 14	
Cither	8 (42)	13 (6.8)	21 (5.5)	_	
Uninvared	0	3(16)	3 (0 k)		
History of eartheyascular disease					
Yes	111 (52 7)	[10 (57 3)	221 (58.0)	- 78	
No	78 (41 3)	52 (42.7)	(60 (42 N)		
Status rate, y					
<1	+(2.1)	2(10)	6 (L6)	_	
i-5	50 (25 5)	51 (26.6)	101 (26 5)	69	
>5	129 (68 3)	134 (69 8)	263 (69 D)		
Unknown	6 (3.2)	S (2.4)	11 (2.9)		
Prepary diagnosis					
Makemant barror	B4 (44.4)	102 (53 1)	186 (48 S)	04	
Other	105 (55 6)	90 (46.91	(95 (51.2)		
0 1 0 114-114-114-114	18(29)	4.9 (2.7)	49(28)	67	

	No. (%)				
Variable	Discentinued Statto (x = 101)	Continued Statio (a = 192)	Tetal (N = 381)	P Value	
AKPS more, mean (SD)	52.4 (13.2)	\$4.5 (12.R)	53 5 (13 0)	IJ	
Copyriterity aspaired					
Yes	51 (27.0)	33 (17.2)	84 (22.01	. m	
No	[38 (73 P)	159 (\$2.8)	297 (78 D)	112	
Emolled in hospice					
Ya	63 (33.3)	74 (38.5)	(37 (36.0)		
Na	124 (65 6)	115 (59 9)	239 (62 7)	.27	
Unknown	2(11)	\$ (1.6)	5 (4.3)		
Neustates medicatines, mean (SD)	11.6 (5.1)	11 5 (4.9)	11.6 (5.0)	84	

1659 Patients screened for eligibility

662 Eligible

381 Enrolled and randomize

and the second of the second o	
7 Withdrawals	3 Withdrawats ⁵
3 Patient decision	1 Patient decision
1 Family decision	2 Family decision
1 Physician decision	
I Incorrect eligibility	
I Unknown	
•	•
182 Included in the primary analysis	189 included in the primary analysis?
8B Cied	98 Died
67 Had < 1 y of participation	70 Had <1 y of participation
27 Had 1 y of participation	21 Had I v of participation

Figure 1. CONSORT Flow Diagram A total of JB9 patients were random Distribution of withdrawals between study arms; P= .85. 75 100 125 150 175 200 725 250 275 300 325 350 375

Davs. No

bands for the continuation arm of the study; light brown shading, the 90% confidence band

No. at risk Continued statin therapy

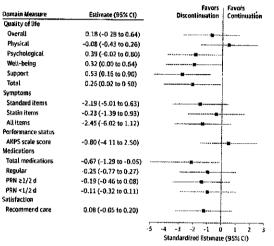


Figure 3. Smannery of Patient-Reported Outcomes In this visual summary of Table 3, the estimates and 95% CIs are presented using idardized units so that the CI widths are comparable; results favoring dis statio therapy are aligned on the left side of zero. The numeric estimates and 95% CIs are presented in the units of the notual analyses, thereby aligning with Table 3. AKPS indicates Australia-Modified Kamofaky Performance Status; PRN, administered as needed.

AUC Difference

0.18 (=0.28 to 0.64) 44

-0 08 (-0.43 (a 0.26) 64

9.39 (-0.02 to 0.00) 06

0.32 (0.00 to 0.64) ns

0.53 (0.16 to 0.90) (tas

U.26 (6 02 to 0 50) 04

-7.2 (-5.0 to 0.6) .13

-0.2 (-1 4 to 0.9) 71

-2.5 (-6.0 to 6.1) LS

-0.2 (-4.1 to 2.5) .63

-0.7 (-13 to -0.); 03

−0.3 (−0.8 to 0,3) 34

-0.2 (-0.5 to 0 t) 16

-0.1 (-0.3 (p·0.1) 33

		Mesa AUC	
Voriable	Baseline	Discoutinged States (n = 159)	Continued
Quality of life			
Overall	6.12	653	
Physical	5.19	5 43	
Psychological	7.21	735	
Well-hong	7.30	7 37	7
Support	(U)	1.38	1
Total	6.98	713	
Synaptourus			****
Standard	27.2	25.2	2
Statin árems	71	7.0	-
All steppes	34.6	32 4	3
AKPS ICOID	54.3	47.7	4
Novatatin medications			
Total	10.9	10.1	10
Regular	8.9	8.4	

		Mess AUC		VAC Dillinance	
Variable	Pareline	Discontinued Statio (p = 125)	Captioned Statts (n = 192)	Estimated (95% CI)	# Voter
Color (between much come describes on recommend)	4 55	4.63	4.55	(LUK (-0.05 to 0.20)	.23

	Cost Smings, 5		
Variable	Prescribed	Generic Formulation Only	
Mean survival, d	212.6	212 6	
Mesos seved per patient			
Days	3.37	2.96	
During meso lifespan in this trial	786.46	629 30	
Projected named US savings			
2014 Population, million	603	529	
2040 Pepulation, billion	-	579	