

Risk of myocardial infarction attributable to abacavir: Analysis to assess the number needed to treat to harm

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Background:

Recently the D:A:D study group reported an increased risk of myocardial infarction (MI) in patients on abacavir, i.e. an adjusted relative risk of 1.90 for an MI compared with patients not receiving abacavir (1). However, in absolute terms the difference in overall incidence rate of an MI was modest - 6.1/1000 PYFU for patients receiving abacavir compared with 2.6/1000 PYFU among those not receiving abacavir. Here we investigated abacavir attributable risk in relation to the underlying risk of MI, expressed as numbers needed to treat to harm (NNTH).

Methods:

The NNTH was calculated as the reciprocal of absolute risk increase (ARI) defined as the difference between the underlying risk of MI with and without abacavir use. The underlying risk of MI was calculated with a parametric statistical model based on the Framingham Heart Study population, estimating the probability of MI over 5 years. The NNTH was calculated as:

$$1 / [(MI\ risk \times 1.9) - MI\ risk]$$

As the Framingham equation is limited to predicting chosen cardiovascular risk over a minimum of 4 and maximum of 12 years time period and the median follow-up time for patients in the D:A:D study was 5.1 years per person, we chose to present the probability of MI occurring within the next 5 years.

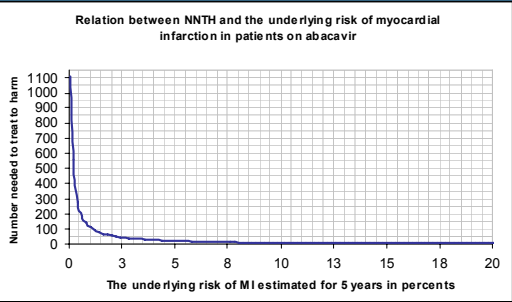
Three patient groups were defined to reflect low (<5%), moderate (5-10%) and high underlying risk of MI (>10%). All NNTH values represent the number of patients which need to be treated with abacavir for 5 years to observe an MI in one additional patient as a consequence of this treatment. A high NNTH represents a small ARI related to abacavir use and a low NNTH represents a large ARI.

References:

1. Sabin C et al. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. Lancet. 2008;371:1417-26.
2. Anderson KM et al. Cardiovascular disease risk profiles. Am Heart J 1991;121: 293-298



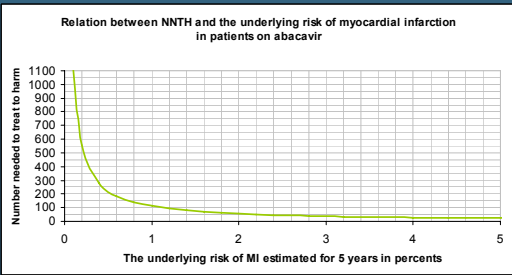
Figure 1. Relation between the NNTH and the underlying risk of myocardial infarction in patients on abacavir



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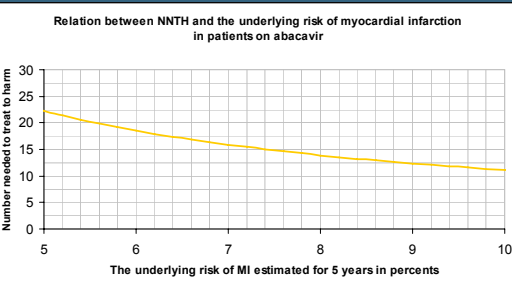
Figure 2. Low risk group



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Figure 3. Medium risk group



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Results:

The graph in figure 1 presents the relationship between the NNTH and the underlying risk of MI. For example, if the underlying risk of MI is 5% the NNTH is 22, meaning that we need to treat 22 patients with an underlying 5-year risk of 5% to observe an MI in one patient.

The graph (fig.1) shows a steep decrease in NNTH with increasing underlying risk, declining from 1111 for the underlying risk of MI of 0.1% to as low as 5 for the underlying risk of MI of 20%.

The low risk group (fig.2) showed the most variation with over a 20-fold drop in NNTH from 1111 to 55 with the underlying risk of MI of 0.1 and 2% respectively. The variation in NNTH was lower within the medium risk group, with a 2-fold decrease in NNTH from 22 to 11 when the underlying risk of MI increased from 5 to 10% (fig.3). In the high risk group the NNTH is small, with small decreases as the underlying risk of MI increased; the NNTH increased from 11 to 5 as the underlying risk of MI increased from 10 to 20% (fig.4).

Figure 5 presents example NNTH values calculated for increasing underlying risk of MI, with contributed risk factors described. The underlying risk of MI presented in the table was calculated with an on-line tool available at www.cphiv.dk (fig6).

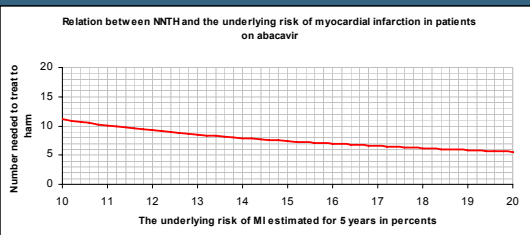
Conclusions:

We demonstrate that it is possible to increase NNTH values for patients on abacavir by decreasing the underlying risk of MI.

The clinical implication for this is simple – by regular screening for and proper managing of existing cardiovascular risk factors in HIV-1 infected patients we are able to increase the number of patients treated with abacavir without having a higher proportion of patients with a negative effect of the drug.

As expected, the lowest NNTH values were observed in the high MI risk group, underlying the urgent need for risk lowering interventions in patients with the underlying risk of MI above 10%. However the most variation in abacavir attributable risk was noted within the lowest risk group. This group of patients should not be disregarded in decision-making, as it represents the largest proportion of HIV-1 infected patients.

Figure 4. High risk group



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Figure 5. Impact of lowering the underlying risk of MI on NNTH

Intervention taken	Underlying risk of MI in 5 years	NNTH
Baseline	6.4%	17
Lowering TCHOL to 170 mg/dL	3.7%	30
Lowering sBP to 120 mmHg	3.1%	35
Increasing HDL to 60 mg/dL	2.6%	42
Introducing smoking cessation	2.2%	50
Both TCHOL and HDL favourable as above	1.3%	85
All parameters changed as above	0.1%	1111

Baseline:
• 40-years- old male
• smoking
• non diabetic
• no ECG-LVE
• sBP 160 mmHg
• total cholesterol 240 mg/dL (6.2mmol/L)
• HDL 35 mg/dL (0.9 mmol/L)

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Figure 6. Assessing individual risk of myocardial infarction with an on-line tool

The risk during the next:
5 years 10 years
Of CHD Is: 0.5% 1.4%
Of CVD Is: 0.6% 1.9%
Of MI Is: 0.1% 0.3%

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