Supplementary Material

 **Supplementary Table 1. Questionnaire for Professionals**

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| **SOCIODEMOGRAPHIC VARIABLES** |
| **Age: \_\_\_\_\_\_\_\_\_\_\_\_years** |
| **Gender:**□ Man□ Woman |
| **Time practicing the profession? \_\_\_\_\_\_\_ years** |
| **Personal history of atherogenic dyslipidemia (have you been diagnosed or treated for atherogenic dyslipidemia?):**□Yes □No |
| **Approximate number of patients with atherogenic dyslipidemia that visits per month: \_\_\_\_\_\_\_\_** |
| **Province where you practice: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| **In what sort of area is your healthcare center located?**□ Rural area (<5,000 inhabitants)□ Semi-urban area (5,000-19,999 inhabitants)□ Urban area (≥20,000 inhabitants) |
| **RESIDUAL CARDIOVASCULAR RISK** |
| **1.1 Do you evaluate residual cardiovascular risk in your routine clinical practice?**□ Yes, but only in patients in secondary prevention.□ I’m not sure what residual cardiovascular risk is.□ Yes, whenever I remember. □ No, because residual risk is a theoretical concept with no clinical impact. |
| **1.2 What do you think lipid-related residual cardiovascular risk refers to?**□ The risk that persists after controlling the patient’s weight.□ The risk that persists after treating the patient with statins and achieving LDL-C objectives.□ The risk that persists after controlling all modifiable risk factors.□ The risk that persists after quitting smoking as a major risk factor. |
| **1.3 To what do you attribute lipid-related residual cardiovascular risk?**□ Age.□ Arterial hypertension. □ Obesity.□ Atherogenic dyslipidemia. |

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| **ATHEROGENIC DYSLIPIDEMIA** |
| **2.1 In your opinion, what are the characteristics of atherogenic dyslipidemia?**□ Elevated LDL-C.□ Normal or moderately elevated LDL-C levels and a phenotype of small, dense LDL-C particles.□ Low HDL-C and elevated triglycerides (TG). □ Low HDL-C, elevated TG, and elevated small, dense LDL-C particles. |
| **2.2 Please indicate any phenotype you think is associated with atherogenic dyslipidemia:**□ Early coronary disease.□ Metabolic syndrome.□ Type 2 diabetes.□ All of the above. |
| **2.3 Please tick the statement that you think is the most accurate:**□ AD is not associated with a high or very high cardiovascular risk.□ AD is of no particular importance in type 2 diabetes, either with regard to macrovascular or microvascular complications. □ AD is a determinant factor for cardiovascular risk, even if LDL-C levels are correct.□ AD does not occur in obese patients.  |
| **2.4 What prompts you to specifically assess AD in your clinical practice?**□ Because cardiovascular risk is increased.□ Because cardiovascular risk is increased by concomitant obesity.□ Because treatment with fibrates must be given.□ Because if it occurs along with diabetes, it should always be treated with insulin. |
| **ATHEROGENIC DYSLIPIDEMIA DIAGNOSIS** |
| **3.1 What parts of the lipid profile do you consider essential for evaluating a patient with atherogenic dyslipidemia?**□ Total cholesterol.□ Total cholesterol and HDL-C.□ Total cholesterol, TG, and HDL-C.□ Total cholesterol, TG, HDL-C, LDL-C and non-HDL cholesterol. |
| **3.2 In a 58-year-old man with a diagnosis of metabolic syndrome, what would be the target for lipid control?**□ Triglycerides.□ HDL-C.□ LDL-C.□ Non-HDL cholesterol. |
| **3.3 In your clinical practice, can you request fractionated total cholesterol to assess HDL-C and LDL-C?**□ No.□ Yes, but I am guided by total cholesterol only.□ Yes, but by referring the patient.□ Yes, routinely and without restrictions. |
| **3.4 How often do you use the following lipoprotein ratios? Considering 1: never; 2: almost never; 3: sometimes; 4: often; 5: very often.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Never** | **Almost never** | **Sometimes** | **Often** | **Very often** |
| **TC/HDL-C ratio** |  |  |  |  |  |
| **LDL-C/HDL-C ratio** |  |  |  |  |  |
| **ApoB/ApoA1 ratio** |  |  |  |  |  |
| **Non-HDL-C/HDL-C ratio** |  |  |  |  |  |
| **TG/HDL-C ratio** |  |  |  |  |  |
| **LDL-C/ApoB ratio** |  |  |  |  |  |

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| **3.5 Please indicate how useful each of the atherogenic indexes is in clinical practice, even if you do not use them (Considering 1: not useful and 5: very useful)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Not useful** | **Of little use** | **Useful** | **Very useful** |
| **TC/HDL-C ratio** |  |  |  |  |
| **LDL-C/HDL-C ratio** |  |  |  |  |
| **ApoB/ApoA1 ratio** |  |  |  |  |
| **Non-HDL-C/HDL-C ratio** |  |  |  |  |
| **TG/HDL-C ratio** |  |  |  |  |
| **LDL-C/ApoB ratio** |  |  |  |  |

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| **ATHEROGENIC DYSLIPIDEMIA TREATMENT** |
| **4.1 What do you think should be the first step in the treatment of atherogenic dyslipidemia?**□ A diet adapted to achieve an appropriate BMI.□ In addition to diet, smoking cessation, if applicable.□ The above, plus regular physical exercise.□ Diet, regular physical exercise, quitting smoking, and pharmacological treatment, if necessary.  |
| **4.2 How would you approach a patient with atherogenic dyslipidemia associated with obesity?**□ Refer the patient to the nurse.□ Refer the patient to the endocrinologist.□ Treat the patient in conjunction with the nursing staff.□ I emphasize the importance of lifestyle changes and I evaluate the use of pharmacological treatment. |
| **4.3 Please indicate how far you agree with each of the following statements about treatment with statins.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |
| **Statins eliminate all residual cardiovascular risk if target LDL-C levels are achieved.** |  |  |  |  |  |
| **Pravastatin has an active hepatic metabolism and should not be used in poly-treated patients.** |  |  |  |  |  |
| **The residual risk associated with high triglycerides and/or low HDL-C is not eliminated with statins alone.** |  |  |  |  |  |
| **If correctly undertaken, diet and quitting smoking are generally sufficient to eliminate the residual risk.** |  |  |  |  |  |

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| **4.4 How would you manage a patient with slightly elevated LDL-C, low HDL-C, and TG over 150 mg/dl, who cannot achieve lipid control with a statin?**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |
| **I would double the dose of statins.**  |  |  |  |  |  |
| **I would add ezetimibe.** |  |  |  |  |  |
| **I would add nicotinic acid.** |  |  |  |  |  |
| **I would add a fibrate.** |  |  |  |  |  |
| **I would add exchange resins.** |  |  |  |  |  |

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| **4.5 What treatment do you think is the most appropriate for managing low HDL-C?**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Not useful** | **Of little use** | **Useful** | **Very useful** |
| **Fibrates.** |  |  |  |  |
| **Statins.** |  |  |  |  |
| **Omega-3.** |  |  |  |  |
| **Nicotinic acid.** |  |  |  |  |

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| **4.6 With regard to TG, please indicate how much you agree with the following statements:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |
| **They are not a cardiovascular risk “per se”.** |  |  |  |  |  |
| **They are a cardiovascular risk factor when they are associated with other abnormal lipid parameters.** |  |  |  |  |  |
| **They are an independent cardiovascular risk factor.** |  |  |  |  |  |

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| **4.7 Please indicate which statement you think is correct:**□ Overall control of the lipid profile in a patient with AD usually needs combined lipid-lowering treatment.□ Administering fibrates to patients with type 2 diabetes mellitus reduces macro and microvascular complications, if they already present.□ The ACCORD study showed that treating AD in diabetic patients conferred a benefit in cardiovascular prevention.□ All the above statements seem correct to me. |
| **4.8 Which fibrate, in your opinion, is the most appropriate for combination with statins:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |
| **Gemfibrozil is the most appropriate fibrate for combination with statins.** |  |  |  |  |  |
| **Fenofibrate is the most appropriate fibrate for combination with statins.** |  |  |  |  |  |
| **Either of the two.**  |  |  |  |  |  |
| **Fibrates must not be used concomitantly with statins.** |  |  |  |  |  |

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| **4.9 A 67-year-old man with acute coronary syndrome without ST elevation (NSTE-ACS), DM2, and obesity, receiving treatment with atorvastatin 80 mg, has the following lipid profile: LDL-C 66 mg/dl, TG 260 mg/dl, and HDL-C 36 mg/dl. Please indicate how you would manage this patient:**□ Target LDL-C has been achieved so the residual cardiovascular risk has been reduced.□ The patient has no residual risk and does not need treatment.□ The patient has AD and a fibrate should be added.□ A fibrate must never be associated with a statin at these doses. |
| **4.10 If your patient has atherogenic dyslipidemia, what is the treatment?**□ Statin + fibrate from the start.□ High-dose statin and once target LDL-C is achieved, evaluate another drug.□ Statin and nicotinic acid.□ Begin with a fibrate and evaluate a statin if targets are not achieved. |
| **4.11 Which of the following statements do you NOT consider correct?**□ Controlling overall lipid profile in patients with AD quite often needs combined lipid-lowering treatment.□ Fenofibrate is the drug of choice for combination with statins.□ Gemfibrozil is the drug with least potential for interactions when used in combination with statins.□ Fibrates are the treatment of choice for treating hypertriglyceridemia. |

**Supplementary Table 2. Residual cardiovascular risk**

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| **Do you evaluate residual cardiovascular risk in your routine clinical practice?** | **n** | **Percentage** |
| Yes, but only in patients in secondary prevention | 287 | 27.89% |
| I’m not sure what residual cardiovascular risk is | 113 | 10.98% |
| Yes, whenever I remember | 623 | 60.54% |
| No, because residual risk is a theoretical concept with no clinical impact | 6 | 0.58% |
| Total | 1029 | 100.00% |
| **What do you think lipid-related residual cardiovascular risk refers to?** | **n** | **Percentage** |
| The risk that persists after controlling the patient’s weight | 6 | 0.58% |
| The risk that persists after treating the patient with statins and achieving LDL-C objectives | 654 | 63.56% |
| The risk that persists after controlling all modifiable risk factors | 368 | 35.76% |
| The risk that persists after quitting smoking as a major risk factor | 1 | 0.10% |
| Total | 1029 | 100.00% |
| **To what do you attribute lipid-related residual cardiovascular risk?** | **n** | **Percentage** |
| Age | 12 | 1.17% |
| Arterial hypertension | 6 | 0.58% |
| Obesity | 23 | 2.24% |
| AD | 988 | 96.02% |
| Total | 1029 | 100.00% |

LDL-C: cholesterol transported by low-density lipoproteins; AD: atherogenic dyslipidemia.

**Supplementary Table 3. Atherogenic dyslipidemia. General aspects**

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| --- | --- | --- |
| **What are the characteristics of atherogenic dyslipidemia?** | **n** | **Percentage** |
| **Elevated LDL-C** | 44 | 4.28% |
| **Normal or moderately elevated LDL-C levels and a phenotype of small, dense LDL-C particles** | 68 | 6.61% |
| **Low HDL-C and elevated TG** | 128 | 12.44% |
| **Low HDL-C, elevated TG, and elevated small, dense LDL-C particles** | 789 | 76.68% |
| Total | 1029 | 100.00% |
| **Which phenotype is associated with atherogenic dyslipidemia?** | **n** | **Percentage** |
| **Early coronary disease** | 14 | 1.36% |
| **Metabolic syndrome** | 36 | 3.50% |
| **Type 2 diabetes mellitus** | 22 | 2.14% |
| **All of the above** | 957 | 93.00% |
| Total | 1029 | 100.00% |
| **Which statement do you consider the most accurate?** | **n** | **Percentage** |
| **AD is not associated with a high or very high cardiovascular risk** | 12 | 1.17% |
| **AD is of no particular importance in type 2 diabetes, either with regard to macrovascular or microvascular complications** | 13 | 1.26% |
| **AD is a determinant factor for cardiovascular risk, even if LDL-C levels are correct** | 998 | 96.99% |
| **AD does not occur in obese patients** | 6 | 0.58% |
| Total | 1029 | 100.00% |
| **What prompts you to specifically assess atherogenic dyslipidemia in your clinical practice?** | **n** | **Percentage** |
| **Cardiovascular risk is increased** | 901 | 87.56% |
| **Cardiovascular risk is increased by concomitant obesity** | 61 | 5.93% |
| **Treatment with fibrates must be given** | 65 | 6.32% |
| **If it occurs along with diabetes, it should always be treated with insulin** | 2 | 0.19% |
| Total | 1029 | 100.00% |

LDL-C: cholesterol transported by low-density lipoproteins; HDL-C: cholesterol transported by high-density lipoproteins; TG:triglycerides. AD: atherogenic dyslipidemia**;**

**Supplementary Table 4 A. Diagnosis of atherogenic dyslipidemia**

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| **What parts of the lipid profile do you consider essential for evaluating a patient with atherogenic dyslipidemia?** | **n** | **Percentage** |
| Total cholesterol | 3 | 0.29% |
| Total cholesterol and HDL-C | 13 | 1.26% |
| Total cholesterol, TG, and HDL-C | 167 | 16.23% |
| Total cholesterol, TG, HDL-C, LDL-C and non-HDL cholesterol. | 846 | 82.22% |
| Total | 1029 | 100.00% |
| **In your clinical practice, can you request fractionated total cholesterol to assess HDL-C and LDL-C?** | **n** | **Percentage** |
| No | 38 | 3,69% |
| Yes, but I am guided by total cholesterol only | 15 | 1.46% |
| Yes, but by referring the patient | 12 | 1.17% |
| Yes, routinely and without restrictions | 964 | 93.68% |
| Total | 1029 | 100.00% |

HDL-C: cholesterol transported by high-density lipoproteins; TG:triglycerides; LDL-C: cholesterol transported by low-density lipoproteins.

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| **How often do you use the following lipoprotein ratios?** |
| **Ratios** | **Never** | **Almost never** | **Sometimes** | **Often** | **Very often** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **TC / HDL-C** | 134 ; 13.02% | 124 ; 12.05% | 225 ; 21.87% | 302 ; 29.35% | 244 ; 23.71% | 1029 |
| **LDL-C / HDL-C** | 149 ; 14.48% | 143 ; 13.90% | 227 ; 22.06% | 294 ; 28.57% | 216 ; 20.99% | 1029 |
| **ApoB / ApoAI** | 617 ; 59.96% | 253 ; 24.59% | 112 ; 10.88% | 34 ; 3.30% | 13 ; 1.26% | 1029 |
| **Non-HDL-C / HDL-C** | 447 ; 43.44% | 271 ; 26.34% | 200 ; 19.44% | 71 ; 6.90% | 40 ; 3.89% | 1029 |
| **TG / HDL-C** | 277 ; 26.92% | 213 ; 20.70% | 250 ; 24.30% | 180 ; 17.49% | 109 ; 10.59% | 1029 |
| **LDL-C / ApoB** | 621 ; 60.35% | 260 ; 25.27% | 99 ; 9.62% | 36 ; 3.50% | 13 ; 1.26% | 1029 |

**Supplementary Table 4 B. Diagnosis of atherogenic dyslipidemia: ratios**

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| **How useful is each of the following atherogenic indexes in clinical practice, even if you do not use them?** |
| **Ratios** | **Not useful** | **Of little use** | **Useful** | **Very useful** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **TC / HDL-C** | 25 ; 2.43% | 116 ; 11.27% | 509 ; 49.47% | 379 ; 36.83% | 1029 |
| **LDL-C / HDL-C** | 29 ; 2.82% | 125 ; 12.15% | 470 ; 45.68% | 405 ; 39.36% | 1029 |
| **ApoB / ApoAI** | 94 ; 9.14% | 324 ; 31.49% | 444 ; 43.15% | 167 ; 16.23% | 1029 |
| **Non-HDL-C / HDL-C** | 88 ; 8.55% | 325 ; 31.58% | 483 ; 46.94% | 133 ; 12.93% | 1029 |
| **TG / HDL-C** | 62 ; 6.03% | 254 ; 24.68% | 464 ; 45.09% | 249 ; 24.20% | 1029 |
| **LDL-C / ApoB** | 107 ; 10.40% | 347 ; 33.72% | 434 ; 42.18% | 141 ; 13.70% | 1029 |

TC: total cholesterol; LDL-C: cholesterol transported by low-density lipoproteins; HDL-C: cholesterol transported by high-density lipoproteins; ApoB: Apolipoprotein B; ApoA1: Apolipoprotein A1; TG:triglycerides.

**Supplementary** **Table 5. Treatment of atherogenic dyslipidemia**

|  |  |  |
| --- | --- | --- |
| **What do you think should be the first step in the treatment of atherogenic dyslipidemia?** | **n** | **Percentage** |
| **A diet adapted to achieve an appropriate BMI** | 6 | 0.58% |
| **In addition to diet, smoking cessation, if applicable** | 4 | 0.39% |
| **The above, plus regular physical exercise** | 35 | 3.40% |
| **Diet, regular physical exercise, quitting smoking, and pharmacological treatment, if necessary** | 984 | 95.63% |
| Total | 1029 | 100.00% |
| **How would you approach a patient with atherogenic dyslipidemia associated with obesity?** | **n** | **Percentage** |
| **Refer the patient to the nurse** | 4 | 0.39% |
| **Refer the patient to the endocrinologist** | 27 | 2.62% |
| **Treat the patient in conjunction with the nursing staff** | 237 | 23.03% |
| **I emphasize the importance of lifestyle changes and I evaluate the use of pharmacological treatment** | 761 | 73.96% |
| Total | 1029 | 100.00% |
| **Treatment with statins: how far you agree with each of the following statements?** |
| **Statements** | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **Statins eliminate all residual cardiovascular risk if target LDL-C levels are achieved** | 252 ; 24.49% | 246 ; 23.91% | 39 ; 3.79% | 411 ; 39.94% | 81 ; 7.87% | 1029 |
| **Pravastatin has an active hepatic metabolism and should not be used in poly-treated patients”** | 437 ; 42.47% | 306 ; 29.74% | 92 ; 8.94% | 150 ; 14.58% | 44 ; 4.28% | 1029 |
| **The residual risk associated with high TGs and/or low HDL-C is not eliminated with statins alone** | 25 ; 2.43% | 38 ; 3.69% | 24 ; 2.33% | 287 ; 27.89% | 655 ; 63.65% | 1029 |
| **If correctly undertaken, diet and quitting smoking are generally sufficient to eliminate the residual risk** | 254 ; 24.68% | 402 ; 39.07% | 60 ; 5.83% | 286 ; 27.79% | 27 ; 2.62% | 1029 |
| **What treatment do you think is the most appropriate for managing low HDL-C?** |
| **Options** | **Not useful** | **Of little use** | **Useful** | **Very useful** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **Fibrates** | 72 ; 7.00% | 260 ; 25.27% | 413 ; 40.14% | 284 ; 27.60% | 1029 |
| **Statins** | 62 ; 6.03% | 303 ; 29.45% | 443 ; 43.05% | 221 ; 21.48% | 1029 |
| **Omega-3** | 59 ; 5.73% | 299 ; 29.06% | 498 ; 48.40% | 173 ; 16.81% | 1029 |
| **Nicotinic acid** | 167 ; 16.23% | 559 ; 54.32% | 243 ; 23.62% | 60 ; 5.83% | 1029 |
| **With regard to TG, please indicate how much you agree with the following statements:** |
| **Options** | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **They are not a cardiovascular risk factor “per se”** | 434 ; 42.18% | 322 ; 31.29% | 58 ; 5.64% | 162 ; 15.74% | 53 ; 5.15% | 1029 |
| **They are a cardiovascular risk factor when they are associated with other abnormal lipid parameters** | 67 ; 6.51% | 93 ; 9.04% | 26 ; 2.53% | 353 ; 34.31% | 490 ; 47.62% | 1029 |
| **They are an independent cardiovascular risk factor** | 61 ; 5.93% | 138 ; 13.41% | 116 ; 11.27% | 354 ; 34.40% | 360 ; 34.99% | 1029 |
| **Please indicate which statement you think is correct:** | **n** | **Percentage** |
| **Overall control of the lipid profile in a patient with AD usually needs combined lipid-lowering treatment** | 44 | 4.28% |
| **Administering fibrates to patients with type 2 diabetes mellitus reduces macro and microvascular complications, if they already present** | 1 | 0.10% |
| **The ACCORD study showed that treating AD in diabetic patients conferred a benefit in cardiovascular prevention** | 13 | 1.26% |
| **All the above statements seem correct to me** | 971 | 94.36% |
| Total | 1029 | 100.00% |
| **Which fibrate, in your opinion, is the most appropriate for combination with statins?** |
| **Options** | **Completely disagree** | **Partially disagree** | **Indifferent** | **Partially agree** | **Completely agree** |  |
| **n ; %** | **n ; %** | **n ; %** | **n ; %** | **n ; %** | Total (n) |
| **Gemfibrozil** | 455 ; 44.22% | 239 ; 23.23% | 138 ; 13.41% | 167 ; 16.23% | 30 ; 2.92% | 1029 |
| **Fenofibrate** | 18 ; 1.75% | 18 ; 1.75% | 30 ; 2.92% | 193 ; 18.76% | 770 ; 74.83% | 1029 |
| **Either of the two** | 444 ; 43.15% | 269 ; 26.14% | 143 ; 13.90% | 130 ; 12.63% | 43 ; 4.18% | 1029 |
| **Fibrates must not be used concomitantly with statins** | 743 ; 72.21% | 180 ; 17.49% | 28 ; 2.72% | 56 ; 5.44% | 22 ; 2.14% | 1029 |
| **If your patient has atherogenic dyslipidemia, what is the treatment?** | **n** | **Percentage** |
| **Statin + fibrate from the start** | 720 | 69.97% |
| **High-dose statin and once target LDL-C is achieved, evaluate another drug** | 197 | 19.14% |
| **Statin and nicotinic acid** | 1 | 0.10% |
| **Begin with a fibrate and evaluate a statin if targets are not achieved** | 111 | 10.79% |
| Total | 1029 | 100.00% |
| **Which of the following statements do you not consider correct?** | **n** | **Percentage** |
| **Controlling overall lipid profile in patients with AD quite often needs combined lipid-lowering treatment** | 73 | 7.09% |
| **Fenofibrate is the drug of choice for combination with statins.** | 81 | 7.87% |
| **Gemfibrozil is the drug with least potential for interactions when used in combination with statins** | 833 | 80.95% |
| **Fibrates are the treatment of choice for treating hypertriglyceridemia** | 42 | 4.08% |
| Total | 1029 | 100.00% |

BMI: body mass index LDL-C: cholesterol transported by low-density lipoproteins; TG: triglycerides; HDL-C: cholesterol transported by high-density lipoproteins. AD: atherogenic dyslipidemia