HOW TO TREAT A HIGHLY ACTIVE RRMS PATIENT AFTER ONE DISEASE MODIFYING DRUG (DMD) HAS FAILED? – SUMMARY

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Before answering the question of treatment the terms “highly active patient” and “treatment failure” have to be defined. For both terms the definitions can be either loose or stringent. The stringent definition of a highly active MS patient would be a patient that experiences at least one clinical relapse per year that leads to a permanent clinical deficit. In addition this patients’ MRI should show new lesions and contrast enhancement as a sign of activity of the lesions. The loose definition of an active patient would be a patient that experiences a minor relapse that does not lead to a permanent deficit and that is not paralleled by an increased lesion burden in the MRI. On the other hand treatment failure might be stringently defined as a patient that experiences clinical relapses despite DMD or loosely defined as a patient that is clinically stable but shows progression in the MRI.

In case of patients with active disease according to the stringent criteria one will probably soon escalate the therapy from interferons/copaxone to natalizumab or mitoxantrone. Both treatments showed a good efficacy which is regarded to be superior to baseline therapies. The choice between these two treatments is probably mainly based on the side effect profile of both drugs with the risk of PML in case of natalizumab and cardiotoxicity, increased risk of leukemia and amenorrhea in case of mitoxantrone. Of course there are also new drugs on the horizon that could be used as escalation therapies once they are finally approved: fingolimod and cladribine. For fingolimod there are data from the phase III clinical trials showing that it is superior to Avonex therapy. For cladribine these data are so far missing. Other possibilities for an escalation could be alemtuzumab, rituximab/ocrelizumab, and daclizumab. All these drugs showed excellent results in phase II clinical trials, but results from phase III clinical trials are still pending. Also combination therapies could be envisioned. Phase II clinical trials with a combination of daclizumab/interferon and cladribine/interferon are on the way or already finished with promising results.

The therapeutic options patients with minor disease activity during baseline therapy are manifold. If a patient is on interferon therapy neutralizing antibodies should be checked. If these antibodies are consistently positive treatment should be switched. Data from a small study indicate that switching these patients to copaxone may reduce the relapse rate. If antibodies are negative these patients could be switched to any other baseline therapy. In general, a switch from one interferon to another interferon or increasing the dose of an interferon seemed to be less effective than switching to copaxone although these data are limited.

Taken together, there is ample evidence that patients with disease activity despite baseline therapy can benefit from a switch of the baseline therapy or from an escalation therapy. The choice between switching baseline therapy and escalation is mainly based on disease severity and previous treatment history of the patient. The important clinical task is to identify patients with a suboptimal therapeutic response early during the disease course.