Migraine is a paroxysmal disorder characterised by attacks of headache eventually associated with nausea, vomiting, photophobia, phonophobia, and malaise. A fast-growing, new class of anti-migraine drugs has recently been introduced for the treatment of migraine: the serotonin (5-HT) 1B/1D agonists. Since the introduction of the first representative, sumatriptan, in 1983, several new compounds of this class have been or are about to be approved for clinical use.

The main pharmacokinetic characteristics of triptans are reported in Table 1 [1]. All the triptans are effective in a high proportion of patients with recurrent migraine attacks, but from the clinical perspective consistency of response, sustained response and good tolerability are the areas that may better clinically distinguish among individual triptans [2]. Michel D. Ferrari, in a review on migraine in The Lancet in 1998, defined the “future” problem of choice among the new triptans as the “triptans war” [3]. In fact, comparative literature data are often hard to understand because of lack of standardised measures of efficacy and safety for different doses, different ways of administration and different times from the administration [4]. Besides, few comparative studies have been carried out with triptans other than sumatriptan, almost always taken as a reference (Fig. 1). Indirect comparisons such as meta-analyses only serve as estimates of relative efficacy or safety that cannot substitute the potential usefulness of direct comparative research on a wide population. Moreover, few long-term efficacy and safety studies have been published [5].

Table 2 reports the main pharmacoepidemiological parameters that are needed to evaluate the efficacy and safety of triptans [6, 7]. Compliance may be defined as the extent to which a patient’s behaviour conforms to medical advice [8].
factors that alter drug distribution or metabolism, such as renal or hepatic insufficiency, congestive heart failure, anaemia, and alcoholism [11]. It has also been suggested that a patient who is receiving specific drugs or drugs of a certain class may be prone to having an adverse effect; however, few studies on headache patients are available (Table 1)

**Table 1: Pharmacokinetics of oral triptans. (Modified from [1])**

| Triptan     | $T_{\text{max}}$ (h) | $C_{\text{max}}$ (ng/ml) | $F$ (%) | $t_{1/2}$ | AUC (mg/l h) | Metabolism       |
|-------------|----------------------|---------------------------|---------|-----------|--------------|-----------------|
| Sumatriptan | 50 mg                | 2                         | 31      | 14        | 2            | 118 MAO         |
|             | 100 mg               | 1.5                       | 54      | 14        | 2            | 158 MAO         |
| RizatRIPTAN | 5 mg                 | 1.2                       | 7.8     | 38        | 1.4          | 17.4 MAO-A      |
|             | 10 mg                | 1                         | 19.8    | 40        | 2            | 50 MAO-A        |
| ZolmitRIPTAN| 2.5 mg               | 2                         | 3       | 46        | 2.6          | 17 P450/MAO-A   |
| Naratriptan | 2.5 mg               | 2                         | 12.6    | 74        | 5.5          | 98 Renal/CYP450 |
|             | 5 mg                 | 2                         | 23.9    | 68        | 5.3          | 200 Renal/CYP450|
|             | 10 mg                | 1.5                       | 46.1    | 68        | 5.5          | 387 Renal/CYP450|
| Eletriptan  | 40 mg                | 1.8                       | 82      | 50        | 5.3          | 670 CYP450      |
|             | 80 mg                | 1.4                       | 246     | 50        | 6.3          | 1661 CYP450     |
| FrovatRIPTAN| 2.5 mg               | 3                         | 7       | 29.6      | 25.7         | 94 CYP450       |
|             | 40 mg                | 5                         | 53.4    | 17.5      | 29.7         | 881 CYP450      |
| Almotriptan | 12.5 mg              | 2.5                       | 3       | 49.5      | 3.1          | 80 CYP450/MAO-A |
|             | 25 mg                | 1.46                      | 103     | 69        | 3.19         | 558.5 CYP450/MAO-A|

*AUC*, area under the curve; *MAO*, monoamine oxidase; $T_{\text{max}}$, time to maximum concentration; $C_{\text{max}}$, maximum blood concentration; $F$, bioavailability

A primary reason for poor compliance among patients receiving medications for headache is adverse effects, many of which are dose related. One difficulty is that triptans often causes adverse effects at therapeutic doses. Some risk factors for adverse effects that have been proposed include age [9], number of drugs the patient is receiving [10] and factors that alter drug distribution or metabolism, such as renal or hepatic insufficiency, congestive heart failure, anaemia, and alcoholism [11]. It has also been suggested that a patient who is receiving specific drugs or drugs of a certain class may be prone to having an adverse effect; however, few studies on headache patients are available (Table 1).
Comparing effective dose sizes, triptans seem to differ in their capacity to cause adverse effects without any relation-
ship between adverse effect frequencies and absolute dose
size, logD, or absolute dose-size lipophilicity index (ADLI = absolute dose in mg/LogD). Moreover, because of the trip-
tans’ similar high affinity for the 5-HT1B/1D receptors, adverse effects could be mediated through mechanisms that
are unrelated to the intrinsic efficacy at those receptors [12].

In clinical practice, the choice of a triptan depends on a number of factors. First of all, it must be decided to use a triptan instead of another non-specific painkiller medicine. At the moment a stratified approach for migraine attack therapy is preferred to optimise positive reinforcement due to the efficacy of the therapy; triptans are able to reduce the number of non-responders to usual therapy [13]. In clinical practice, the differences outlined (sometimes with conflicting results) in comparative clinical trials are immediate undetectable, so that the efficacy or safety of different triptans is in many case overlapping for the clinician. In this situation the main point to consider in choos-
ing triptans seems to be the patient’s preference. In fact, the difference in direct costs, in Italy, are almost negligi-
ble, and the difference in preference by patients can be resumed as the following:

1. Rapidity in onset of action;
2. Consistency in repeated use;
3. Mode of administration;
4. Previous use;
5. Incidence of side effects;
6. Counselling of other patients.

Keeping in mind this point, we can identify the more acceptable drug, optimise the compliance and hope to target the maximum therapeutic effect. A well-informed patient is the first step for a good therapeutic strategy.

In conclusion, the most frequent question is: Which is the best triptan? The best answer to this question is that it is the wrong question! In fact, a patient’s expression of treatment reference is a valuable thing to know, not only for the individual’s clinical management, but also at the population level for epidemiological and economic reasons. In agree-
ment with Sheftell and Fox [14], we believe that a good migraine care strategy requires a balance with what the patient views as satisfactory, a reasonable compromise between efficacy and tolerability, and a careful follow-up.

Table 3 Comparison of adverse effects and recurrence with different triptans. Data refer to oral administration unless otherwise indicated

| Drug      | All AE, % | Chest symptoms, % | Recurrence, % |
|-----------|-----------|-------------------|---------------|
| Placebo   | 29–46     | 1–3              | 10–44         |
| Sumatriptan 100 mg | 58      | 5                | 34            |
| Sumatriptan 50 mg | 56      | 5                | 34            |
| Rectal     | 2         | 0                | 22            |
| Naratriptan 6 mg SC | 59      | 5                | 46            |
| Naratriptan 5 mg | 18      | 0.2–1.0          | 32            |
| Zolmitriptan 2.5 mg | 39      | 3                | 26            |
| Rizatriptan 5 mg | 39      | 2                | 38            |
| Rizatriptan 10 mg | 31–47  | 5                | 41            |
| Almotriptan 12.5 mg | 46      | 0.4–2.0          | 18            |
| Elitriptan 40 mg | NR      | 7                | 21            |
| Elitriptan 50 mg | NR      | 7                | 32            |

SC, subcutaneous; AE, adverse events; NR, not reported
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