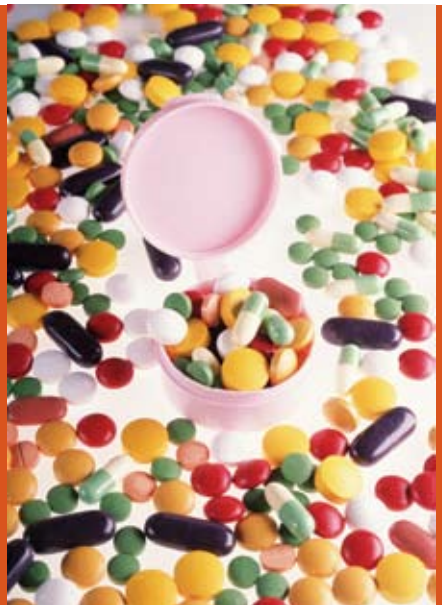

What Makes Innovative Therapy or Off-Label Prescribing Ethically Acceptable and Appropriate?

By Dr T Thirumoorthy

Appropriate treatment refers to the selection of the modality of treatment which is known to deliver the intended result. The choice of such treatment is planned by good clinical judgment, properly administered and achieves its intended result of best possible outcome.

Accepted methods of exercising good clinical judgment in choosing a treatment option includes the use of methods with the best available evidence, the clinical experience of the doctor and incorporating the preferences or the best interests of the patient. Standard approved therapy is most useful for patients with uncomplicated illness, based purely on evidence available from similar patients.

On the other hand, non-standard therapy is needed in complicated, complex illnesses or where standard approved treatments have failed.

Complicated illness and situations are usually not covered in the inclusion criteria of the randomly controlled trials of that therapy. Most clinical trials for drug or device approval are designed to recruit only a small segment of patients with specific inclusion criteria, as compared to the wide variation of clinical features of patients that clinicians usually see in clinical practice. This explains the need for and the common use of innovative therapy and off-label prescriptions in clinical practice.

In assessing whether an innovative therapy or off-label prescribing is ethical, appropriate and thus acceptable, the following criteria needs to be considered –

1. PATIENT PREFERENCES

(Respect for Persons and Patient Autonomy)

Appropriately informed patient. Consent or request from patient and fulfilling the best interest principle. Consent is a continuous process throughout the treatment, and there should be constant updating of the patient of the progress and the option to stop treatment (withdraw consent) at any stage.

2. MEDICAL INDICATIONS

(Goals of Medicine)

(I) The lack of effective standard or recommended therapy;

(II) Rare or uncommon disease where evidence and experience are always inadequate;

(III) Failure of standard therapy and no alternative safe and effective therapy;

(IV) The complexity of the medical situation which does not allow standard therapy or contraindications to standard available therapy;

(V) Serious and complex clinical situations needing innovative approach;

(VI) Where drugs or therapy may save cost and promote convenience or compliance.

3. RISK/BENEFIT ASSESSMENT

(Beneficence/Non-maleficence)

(I) Good prospects of achieving the intended outcome and improving quality of life;

(II) Potential benefits outweigh the risks;

(III) Firm scientific rationale and fundamentally sound to use in the chosen clinical situation;

(IV) Evidence of benefit from anecdotal reports, accepted and used by clinical colleagues. Good evolving evidence of benefit. Publications in peer-reviewed journals;

(V) The drug or device has been approved and used in similar cases or conditions with comparable pathophysiology;

(VI) Extension of clinical use of established or approved therapy based on class effect, for milder or related conditions (for example, administering Singular for chronic obstructive pulmonary disease), to conditions sharing similar physiological linkage (for example, administering Metformin for polycystic ovarian syndrome), to conditions of similar symptom-complex (syndromes);

(VII) Monitoring for risk throughout the treatment.

4. THE CLINICIAN FACTORS

(I) Clinician is well-informed about the drug or device intended for off-label use;

(II) Clinician using the off-label therapy has knowledge, skill and experience of previous use;

(III) Peer review or consultation with an experienced and skilled colleague for exclusion of provider clinician bias or prejudice.

Innovative therapy is closer to medical practice than experimentation. Experimentation is invoked when the evidence is non-existent or evidence of benefit or the lack of is in equipoise. Innovative therapy is not experimental when there is sufficient evidence, whether direct or indirect, and supported by the clinician's experience and patient preference. Innovative therapy is for clinical therapy of a special group of patients whereas experimentation is for the purpose of developing generalisable knowledge.

Accepted methods of exercising good clinical judgment in choosing a treatment option includes the use of methods with the best available evidence, the clinical experience of the doctor and incorporating the preferences or the best interests of the patient.

Current medical care invariably involves patients with multiple co-morbidities, complicated illnesses and features that make standard therapy unsuitable or ineffective. Clinicians are thus constantly called upon to be innovative to relieve the suffering of our patients. Standard and innovative therapies are thus a continuum rather than distinct entities. Innovative therapy is to be encouraged as long as good clinical judgment is exercised and patient's interest preserved.

In conclusion, innovative but unproven or unregistered therapy is ethical when applied to specific situations where standard therapy has not or does not achieve the goals of treatment. It is made ethical with patient consent, preference and/or when the overall best interest of the patient is preserved. Innovative or non-conventional therapy is ethically acceptable where benefits outweigh risk and cost and convenience justifies its use. However at all times when using unconventional or off-label use of drugs or devices, where risk may be unknown or not established, the clinician has a special duty to monitor for adverse reactions and mitigate them in a timely manner. SMA

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