

Supplementary material to:

SELECT A SUITABLE TREATMENT STRATEGY FOR CROHN'S DISEASE: STEP-UP OR TOP-DOWN

Qian-Qian Chen, Li Yan, Jun Wan*

Department of Nanlou Gastroenterology, Chinese PLA General Hospital, Beijing 100853, China

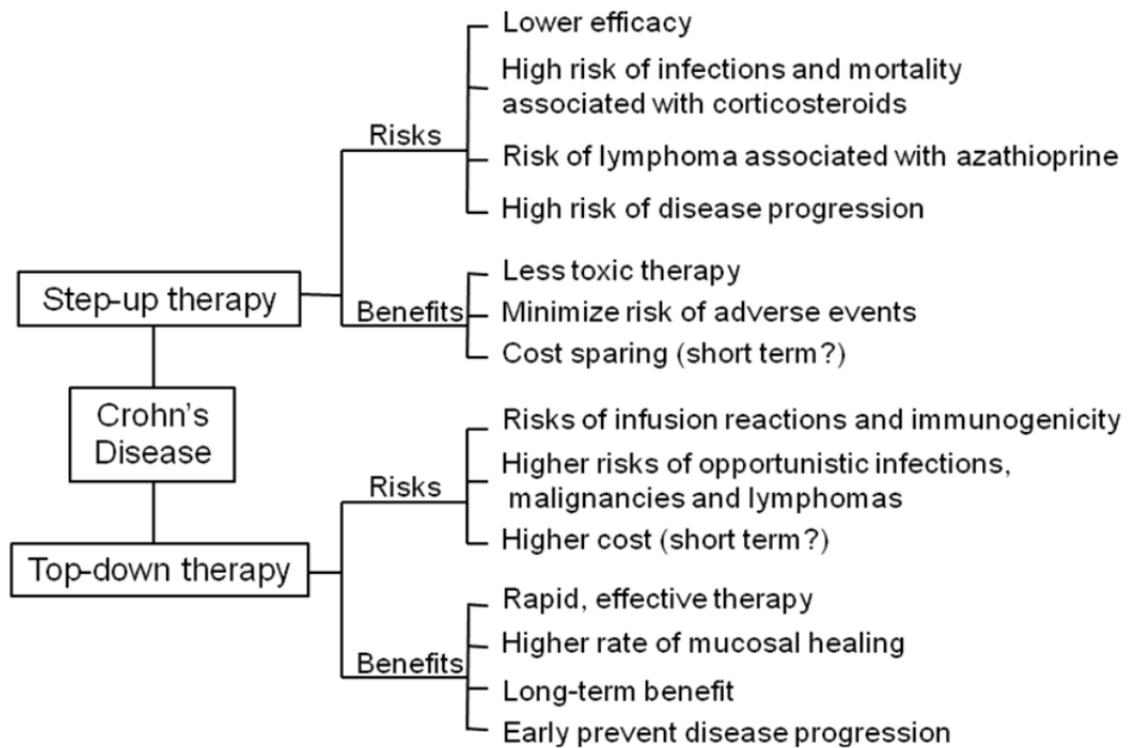
* Corresponding author: e-mail:wanjun301@126.com; phone.: +86-10-66876266;
 Fax: +86-404-68295664.

Supplementary Table 1: Step-up versus top-down therapy

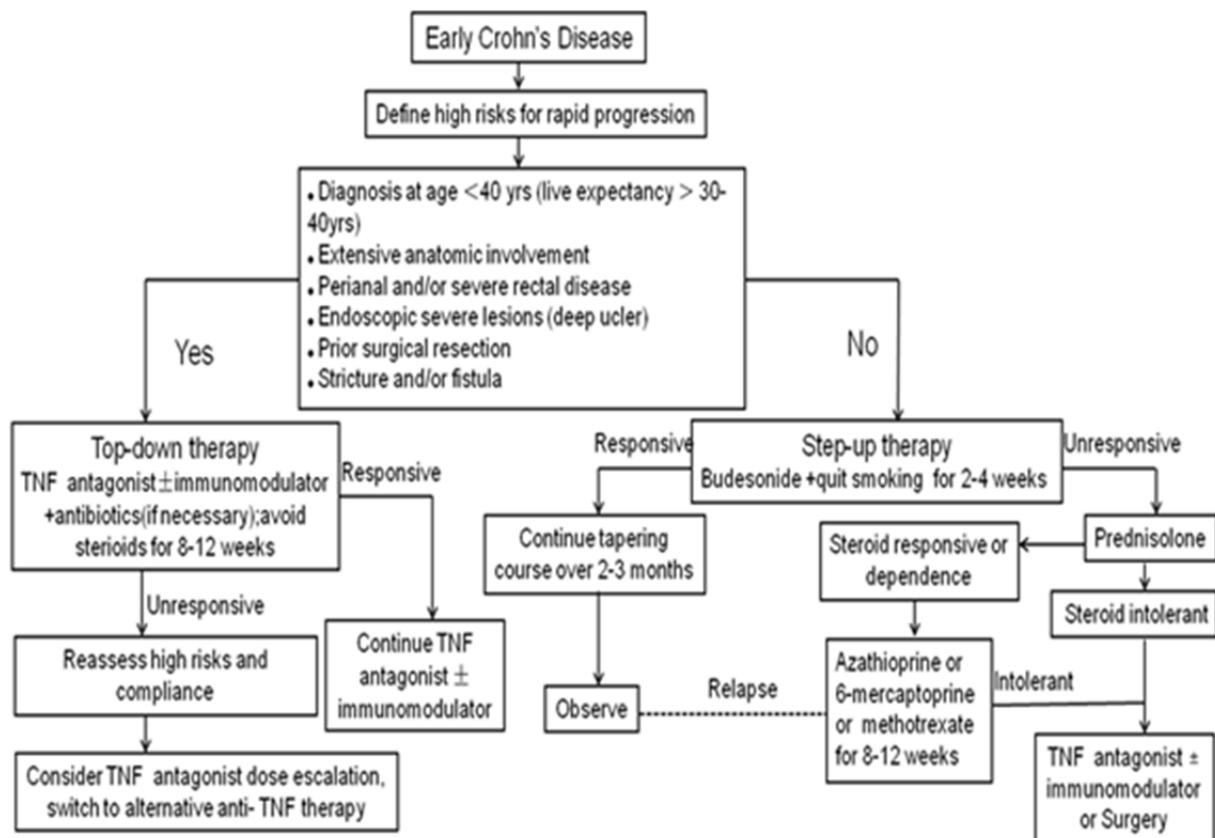
Therapy strategies	Project	Outcomes	Reference
Step-up therapy	corticosteroids, followed sequentially by azathioprine and infliximab	Remission: 26, 39-week (35.9 %), 52-week (42.2 %); Adverse events: 25.3 %	D'Haens et al., 2008
Top-down therapy	three infusions of infliximab (week 0,2,6)+ azathioprine (2.5 mg/kg) per day	Remission: 26, 39-week (60.0 %), 52-week (61.5 %); Adverse events: 30.8 %	
Step-up therapy	prednisolone(1-2 mg/kg) + Mesalamine, (50-80 mg/kg) or azathioprine (2-3 mg/kg) + Infliximab (5 mg/kg) as sequence	Remission: 8-week (27.3 %), 1-year (45.5 %); Adverse events: Leukopenia (9.1 %)	Kim et al., 2011
Top-down therapy	i. v. infusion of infliximab (5 mg/kg at week 0, 2, 6) + azathioprine, repeated every, 8 weeks for 10 months	Remission: 8-week (88.9 %), 1-year (83.3 %); Adverse events: Leukopenia (11.1 %)	
Step-up therapy	corticosteroids, followed sequentially by azathioprine and infliximab	Duration: 49.6 ± 5.2 weeks; Relapse rate: 1-year (50 %), 2-year (90 %), 3-year (90 %)	Yang et al., 2012
Top-down therapy	i.v. infusion of infliximab (5 mg/kg at week 0, 2, 6)+ azathioprine for 1 year; then + azathioprine after 2 years	Duration: 1.8 ± 2.4 weeks; Relapse rate: 1-year (16.7 %), 2-year (50 %), 3-year (61.1 %)	
Step-up therapy	corticosteroids, followed sequentially by azathioprine and infliximab	Remission: 10-week (45.8 %), 30-week (58.3 %); Mucosal healing: 10-week (33.3 %), 30-week (54.2 %) Adverse events: 41.7 %	Xiao et al., 2012
Top-down therapy	three infusions of infliximab (5 mg/kg, week 0, 2, 6) followed by maintenance dosing every 8 weeks beginning at 14-week	Remission: 10-week (70.6 %), 30-week (82.4 %); Mucosal healing: 10-week (35.3 %), 30-week (52.9 %) Adverse events: 29.4 %	

Supplementary Table 2: Treatment strategy guided by ageing

Age range	Disease features	Treatment strategy	Attention	Reference
Children / Adolescents	Anemia, malnutrition, osteopaenia, impaired linear growth, delayed puberty, more likely to have complications	Corticosteroids	Side effects: increased appetite and fluid retention; enhanced bone resorption and decreased new bone formation	Krupoves et al., 2011
		Exclusive enteral nutrition (EEN)	Positive improvements in weight and linear growth, stabilization of bone turnover	Sherlock et al., 2012; Day et al., 2013
		Biological therapies	Improved height velocity, height centile increases, timing prior to early puberty; only infliximab is approved for children	Sprakes et al., 2012; Assa et al., 2013
Adults	Characteristic and extraintestinal symptoms; a risk factor-smoking linked to gender and age at diagnosis, most prominent in adults	Corticosteroids	Use for prolonged periods to control symptoms in steroid-dependent patients; inappropriate in patients with complications	Wolverton et al., 2012
		Biological therapies	Infliximab, adalimumab, certolizumab, natalizumab, sargramostim, a selective adhesion molecule are approved for adult; the efficacy are shown by a large number of studies	Danese, 2012
		Anti-TNF and immuno-modulator combination therapy	Appropriate in patients with short duration of disease, extensive lesions, perianal involvement, females, history of surgery and in older adults; inappropriate in relatively healthy young males.	Melmed et al., 2010
		Stop smoking	Smoking predicts poor outcomes of CD	Lakatos et al., 2013
Elderly > 65 years	Mild clinical course; Less likely to have complications; more likely to have colonic disease location	Care	Improve quality of care as a first step	Charpentier et al., 2013
		Conventional therapy	5-ASA (administrate to almost all); Steroids(40 %)	
		Immuno-suppressives	Higher risk for lymphoma and skin cancer	Beaugerie et al., 2009; Setshedi et al., 2012
		Anti-TNF	High rate of serious infections and mortality	Cottone et al., 2011



Supplementary Figure 1: Risk/ benefit assessment of different treatment strategies



Supplementary Figure 2: Proposed algorithm for treatment of early CD, modified from Ordás et al., 2011; Burger et al., 2011; Yang et al., 2011